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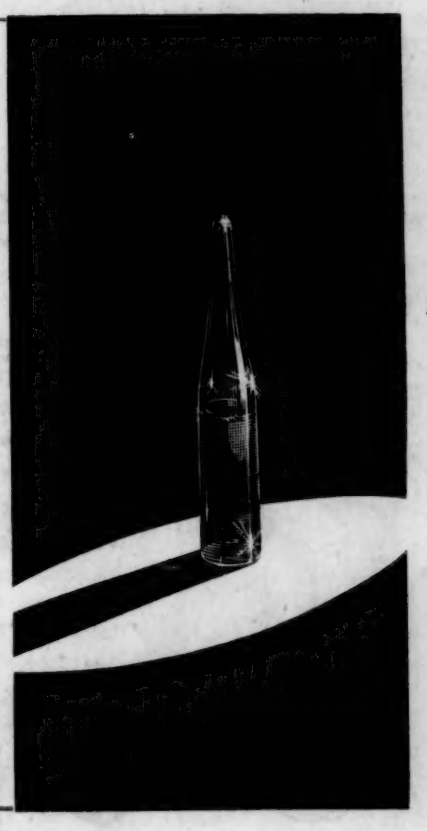

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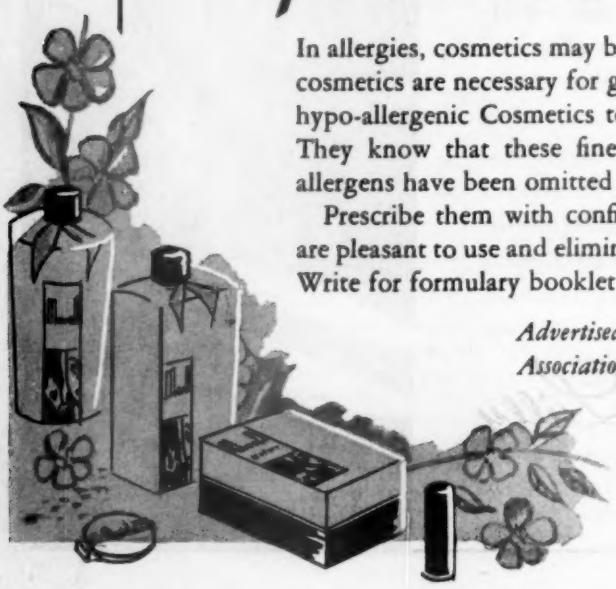

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SEPTICEMIA DUE TO *SALMONELLA ENTERITIDIS*

MYLES P. BAKER, M.D.,* AND JOSEPH H. BRAGDON, M.D.†

BOSTON

THE genus Salmonella comprises a large number of gram-negative enteric bacilli pathogenic to both man and animals. They are grouped together by reason of similarities in biochemical behavior, but more definitively by reason of the specific antigens that they possess in common. Differentiation within the group is based on variations, often minor, in these biochemical and antigenic characteristics. The National Salmonella Center has available for distribution over one hundred and sixty different species or types, not all of which, however, have yet been proved pathogenic to man.[1]

In the accepted classification *Salmonella enteritidis* falls into Group D, for its somatic antigens are identical with those of *Eberthella typhosa*. In most respects, however, it more closely resembles other members of the genus. It has a wide natural distribution, having been isolated from a variety of animals, both wild and domestic, in many parts of the world. Human infections with *S. enteritidis* usually arise from the ingestion of uncooked material from infected animal sources. Persons thus contracting infection with this organism characteristically develop nonbloody and nonpurulent diarrhea accompanied by varying degrees of abdominal pain, nausea and vomiting. Prostration may be alarming, but the symptoms are short lived, and recovery is complete.

S. enteritidis was first isolated in 1888 by Gärtner,[2] who recovered it following an outbreak of acute gastroenteritis that had affected 58 persons, all of whom had eaten meat from an emergency-slaughtered cow. Known since that time as Gärtner's bacillus, it has frequently been responsible for similar outbreaks of food poisoning. In 1926 Kinloch et al.[3] reported an outbreak of acute gastroenteritis in Aberdeen affecting 497 persons, all of whom had drunk milk subsequently traced to a single cow. *S. enteritidis* was isolated from the cow's udder, from samples of the milk and from the stools of many of the victims. According to Topley and Wilson,[4] *S. enteritidis* was responsible for over 12 per cent of all outbreaks of food poisoning produced by Salmonella in England between 1923 and 1939. It was exceeded in incidence only by *S. typhimurium*. An analysis by Edwards and Bruner[5] of data accompanying organisms submitted to the National Salmonella Center indicates that it has been somewhat less frequent in the United States.

Although *S. enteritidis* has definite invasive powers for the tissues of mice and of other laboratory rodents, in human infections it is not prone to penetrate beyond the intestinal mucosa. It is true that Gärtner originally isolated the organism from the spleen of the one fatal case in his series, but comparable cases with adequate bacteriologic confirmation are extremely rare. The literature contains several reports of isolated cases in which *S. enteritidis* was reputedly recovered from the blood stream, but it is likely, as Topley and Wilson[4] point out, that many of these were actually cases of infection with *S. dublin*, whose differentiation is of comparatively recent date. Confusion caused by failure to distinguish the two organisms occurred as late as 1944, when, in an article entitled "*Bacterium enteritidis* Septicaemia," McDonald[6] reported 3 cases of prolonged fever — one of which was fatal — in Indian soldiers. In each case *S. dublin* was isolated from the blood.

Authenticated cases in which *S. enteritidis* has been recovered from sites other than the gastrointestinal tract are, nevertheless, to be found. Of a thousand consecutive Salmonella organisms (exclusive of *E. typhosa*) submitted to the New York Salmonella Center thirty-one were identified as *S. enteritidis*. Seligman, Saphra and Wassermann,[7] in analyzing this material, reported that in 25 cases the organism had originally been isolated from stools, but that in 4 it had been recovered from the blood and in 2 from abscesses; in 1 it had been the cause of a purulent meningitis. Clinical case reports in which *S. enteritidis* has exhibited invasive qualities are confined largely to infants, among whom the organism appears to have a predilection for the meninges. Guthrie and Montgomery[8]

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reported a nursery epidemic involving 27 infants. In 15 cases the organism penetrated the body beyond the intestinal tract, producing a purulent meningitis in 10.

Among adults *S. enteritidis* appears to gain access to the blood stream only when the natural resistance of the host has been lowered by concomitant diseases. Savino and Menendez[9] identified the organism following isolation from the blood of 10 soldiers in the Chaco War. Clinical data in their paper are extremely scanty, but the patients were apparently suffering from a condition similar to typhoid fever. The authors emphasize the point that the troops were severely debilitated by other conditions. Huang et al.[10] reported 17 cases of bacteremia due to *S. enteritidis* among the beggars of Peking. In 9 cases the infection occurred simultaneously with relapsing fever, and in all the authors emphasized the poor general health of the patients.

During the fighting in the Buna-Sanananda area of New Guinea in December, 1942, and January, 1943, a considerable but unknown number of American and Australian troops became infected with *S. enteritidis*. In several cases the organism penetrated beyond the gastrointestinal tract, producing fevers and suppurative processes of considerable clinical interest. It is the purpose of this paper to report 6 cases among American troops, all of whom were seen at a United States Army general hospital at various times following the close of the campaign.*

Case Reports

Case 1. About January 29, 1943, while in combat at Sanananda, this patient developed fever and headache. He was hospitalized. Because of the finding of a positive smear for malaria (type undetermined) and an enlarged spleen, he was given antimalarial therapy. A temperature up to 105°F. continued. At the end of the 1st week of fever the left testicle became painful, simultaneously with the onset of a mild degree of frequency and dysuria.

The patient was evacuated to Australia and on February 24 was admitted to the hospital, exhausted and apathetic. His chief complaints at that time were diarrhea and testicular pain. The temperature was 102.4°F., and the pulse 90. Physical examination revealed an enlarged spleen and a swollen, tender left epididymis. Examination of the blood disclosed a hemoglobin of 60 per cent and a white-cell count of 7000, with a normal differential count. Smears were negative for malaria. The urine persistently showed many polymorphonuclear cells in the sediment. The stools were liquid but not purulent. Although no diagnosis was made, sulfathiazole was given, following which the fever, diarrhea and epididymitis subsided.

On March 3 the patient first complained of pain over the fifth costal cartilage on the right, and during the following 10 days a subcutaneous mass gradually developed in this area. The mass was firm and tender, and the overlying skin was reddened. It was aspirated and from the thin purulent material obtained *S. enteritidis* was isolated in pure culture.

The general condition had continued to improve, but on April 7 the patient again began to have daily elevations in temperature. The right femoral lymph nodes became moderately enlarged and tender. The white-cell count rose to 22,850, with 31 per cent eosinophils, but this was presumably related to the subsequent appearance of hookworm ova in the stools. A blood culture taken on April 13 grew *S. enteritidis*, but one taken on the following day remained sterile. A stool specimen submitted on April 24 was positive for the same organism, and sulfadiazine therapy was begun. The drug was continued for 3 weeks and was associated with a steady decrease in the temperature and a reduction in the size of the femoral nodes. *S. enteritidis*, however, continued to be passed in the stools. The patient was given sulfaguanidine for 16 days, after which repeated cultures remained negative.

The only problem then remaining was a chronic draining sinus on the chest wall, which had been present since a biopsy of the abscess had been taken in April. On August 25 the sinus was explored. It was found to lead into a cavity in the fifth costal cartilage. Six centimeters of cartilage was removed. The wound healed slowly, continuing for some time to give positive cultures for *S. enteritidis*. The patient was not returned to duty until November, almost 10 months after the appearance of the first symptoms.

In March, 1944, the patient was readmitted to the hospital for an unrelated condition. The sinus on the chest wall had remained closed. Two stool cultures were examined for *S. enteritidis* with negative results.

Case 2. This soldier, from the same company as the patient in Case 1, had been in the combat area at Sanananda from December 28, 1942, to January 9, 1943. On January 20 he had his first chill and a fever that did not respond to the usual therapeutic doses of quinine. He was therefore admitted to a hospital, where, because of an enlarged spleen and a smear that was said to have been positive for *Plasmodium vivax*, quinine was continued in large doses. The patient became progressively worse, developing a severe diarrhea, a painful right epididymis and, eventually, delirium. He was evacuated to Australia and admitted to the hospital on February 24.

On admission he was febrile. The spleen was enlarged and tender. The right epididymis was markedly swollen and tender. The white-cell count was 5650, with a normal differential. No malaria parasites were found. The patient was moderately anemic, and there was a mild pyuria. He was treated supportively. The diarrhea soon relented, but left-sided pleuritic pain developed. Rales were heard over the left lower lobe, and an x-ray film confirmed the diagnosis of pneumonitis as well as showing a small pleural effusion. Sulfathiazole was given without effect. Not until March 25 did the patient become afebrile — for the first time in 9 weeks — and begin to improve in weight and well-being. The epididymitis subsided spontaneously.

On April 23 he complained of the sudden onset of severe pain low in the back. About 2 weeks later chills and fever reappeared. *P. vivax* was again demonstrated in the blood, but in spite of intensive antimalarial therapy the fever continued for 4 or 5 weeks. Physical and x-ray examination revealed no localizing signs of infection in the lumbar vertebras. Because of experience with other cases of infection with *S. enteritidis* this organism was specifically sought in the blood, stools and urine, but with negative results. A specimen of serum drawn on May 30, however, agglutinated the organisms recovered from other cases of infection in dilutions of 1:320.

By June 15 the second febrile episode had terminated, and the patient began to regain the 25 pounds of weight that he had lost. He continued, however, to complain of severe low-back pain, and the sedimentation rate remained elevated. It was not until August 16 that there were any radiographic changes to explain these phenomena. At that time definite narrowing of the intervertebral spaces between the fourth and fifth lumbar vertebras, with partial destruction of the posterior portions of the vertebras, was observed. In view of the clinical course and the high agglutinating titer of the serum it was believed that *S. enteritidis* was the organism responsible for the bone infection. The patient was immobilized in a plaster shell, with considerable relief of pain, and evacuated to the United States. The subsequent course of the illness is not known.

*Fourteen similar cases[11] were observed in an Australian general hospital at Port Moresby from January to March, 1943. The patients had been evacuated from the same small combat area from which the following cases had been derived. The predominant clinical picture was that of sustained fever, with urinary-tract infection, septic complications, such as empyema, periostitis and perichondritis (costal cartilage), or subcutaneous abscess. *S. enteritidis* was recovered from the blood, urine, stools and abscesses. In 1 case the soldier had been out of the combat area for a month before the onset of the febrile illness.

CASE 3. In early January, 1943, while in a field hospital near Buna convalescing from a minor gunshot wound received a month previously, this patient had diarrhea and fever for 4 or 5 days. On January 10 malaria parasites (type undetermined) were found in the blood, but despite specific therapy the fever continued unabated for another 12 days. At that time an area of local tenderness on the right lower chest anteriorly was noted. Occasionally, a sharp pain was present in the same region. All symptoms, however, including the fever, gradually subsided.

In February cloudy vision developed in the left eye, and the patient was evacuated to Australia, entering the hospital on the eye service on February 25. Examination revealed fine vitreous opacities with an area of acute choreoretinitis. The eye slowly responded to local treatment.

It was not until April 1 that attention was directed to a tender mass overlying the costochondral junction of the right eighth rib. This corresponded in location to the previous attack of pain and tenderness. In other respects the patient felt entirely well and was afebrile. On April 25 the mass was aspirated, yielding a small amount of purulent material, from which *S. enteritidis* grew in pure culture. Three urine and six stool cultures were negative for the same organism. Sulfadiazine was given for 3 weeks, following which the mass resolved. The patient was discharged to duty in July.

CASE 4. This soldier was in combat in the Buna-Sanananda area from December 5, 1942, to February 4, 1943, his company being for a time close to that of the patients in Cases 1 and 2. During this period he had two bouts of malaria, both of which quickly responded to specific therapy, and one attack of mild diarrhea for 6 days. Following the campaign his unit was returned to Australia. The patient was active on training maneuvers until March 26, when he developed pain in the left shoulder and, 2 days later, chills, fever, abdominal pain and vomiting. He was admitted to a hospital, where malaria parasites were found in the blood. Despite specific therapy the temperature continued to swing daily up to 103°F. The white-cell count remained under 10,000, with a normal differential. Sulfadiazine had no effect on the fever. Finally, a tender mass appeared in the left upper quadrant of the abdomen, and the patient was transferred to a general hospital on April 18.

On admission the patient was febrile. In addition to a grapefruit-sized mass in the left upper quadrant a soft tender mass was palpable in the rectovesical pouch. The white-cell count was 5600. On April 22 the pelvic abscess was evacuated through the anterior rectal wall, and the left upper quadrant mass, which was found to be a well localized peritoneal abscess, was incised and drained. From the latter, *S. enteritidis* was isolated in pure culture.

Following surgical drainage there was a prompt cessation of fever. Blood and urine cultures taken during the following week were sterile, but from two of several stool specimens the same organism was isolated. The patient made an excellent recovery, and the surgical wound healed without evidence of residual infection. Following sulfaguanidine therapy for 11 days, *S. enteritidis* disappeared from the stools.

CASE 5. This patient was in the Buna-Sanananda area from December 25, 1942, to February 12, 1943. During that time he had no diarrhea but did have two attacks of fever, both of which responded to specific antimalarial treatment. In June, while on furlough in Australia, he developed chills, fever and severe backache. Antimalarial treatment had no effect on the symptoms. He became extremely ill, confused and irrational. On June 26 he was transferred to the hospital.

The temperature rose almost daily to 103°F. Physical examination revealed only a palpable spleen and severe low-back pain, with muscle spasm. The white-cell count was 5700, with a normal differential. The urine showed moderate numbers of polymorphonuclear cells. Despite negative smears for malaria therapeutic doses of quinine and quinacrine (Atabrine) were given, but without effect on the fever. Blood-agglutination studies were performed, and the serum was found to agglutinate *S. enteritidis* in a dilution of 1:640. The organism was then isolated from the urine and from the stools. Although "rose spots" appeared on the abdomen, blood cultures remained sterile.

On July 27 sulfaguanidine therapy was instituted. Stool and urine cultures soon became negative, and the temperature returned to normal. X-ray films taken on August 2 showed a destructive process in the body of the fourth lumbar vertebra. The patient remained afebrile, but because of pain he was immobilized in a plaster shell and evacuated to the United States. The subsequent course of the illness is not known.

CASE 6. This patient was in the Buna-Sanananda area from late November to late December, 1942. In the latter month he had two mild attacks of diarrhea, and on December 26 a bout of malaria, with a positive smear, which responded promptly to specific therapy. He had two further attacks of malaria, one in January and one in March, 1943, both of which responded satisfactorily to treatment.

On April 8, while on duty in Australia, he developed pain and swelling in the left testicle. He was afebrile, and there were no systemic symptoms. He was admitted to a hospital, where he received sulfadiazine and applications of ice to the testicle. The pain and swelling gradually subsided, and he was returned to duty. Two days later the same symptoms recurred.

On admission to a general hospital on May 7 he was afebrile. Physical examination revealed no abnormalities other than a tender, moderately enlarged left testis, with some thickening of the cord. Routine laboratory examinations were negative. The white-cell count was 9000.

On May 13 an orchidectomy was performed. The testis was found to be distended by a large abscess filled with thin, gray fluid. *S. enteritidis* was isolated in pure culture from the exudate. Blood and urine cultures were then taken and proved sterile, but on several occasions the stools were found to contain the same organism. Sulfaguanidine therapy was accordingly administered and was followed by the disappearance of the organism from the stool. Complete healing of the surgical wound occurred, and the patient was discharged to duty on October 6.

BACTERIOLOGY

Salmonella organisms grow readily on ordinary bacteriologic mediums, and in most cases a tentative identification can be made within a few days by fermentation reactions and simple group-agglutination tests.* Definitive identification within the group, which depends on minor variations in antigenic structure, should be delegated to laboratories specifically equipped for such work.†

TABLE 1. *Sources of* S. enteritidis *and Maximum Serum Agglutinin Titers.*

CASE NO.	SOURCE				MAXIMUM TITERS
	BLOOD CULTURE	URINE CULTURE	STOOL CULTURE	ABSCESS CULTURE	
1	Positive	Negative	Positive	Positive	1:2560
2	Negative	Negative	Negative	—	1:320
3	—	Negative	Negative	Positive	1:2560
4	Negative	Positive	Positive	Positive	1:640
5	Negative	Positive	Positive	—	1:640
6	Negative	Negative	Positive	Positive	1:80

Table 1 presents the various sources from which the organism was recovered in each case. It should be realized that cultures were rarely taken during

*The biochemical reactions were constant in all cases. The organisms promptly fermented the following sugars with the production of acid and gas; dextrose, maltose, mannite, xylose, arabinose, rhamnose and sorbitol. Dulcitol was fermented only after four or five days. Lactose, saccharose, inosite and inulin were not fermented. The organism produced large amounts of hydrogen sulfide. It did not produce indol or liquefy gelatin.

†We are indebted to Dr. Erich Seligmann, of the Department of Bacteriology, Beth Israel Hospital, New York City, who determined the antigenic structure of the organism.

periods of the infection in which positive results were likeliest to occur — that is, they were obtained for the most part late in the course of the disease.

In a case of vertebral abscess (Case 2) the diagnosis was based only on the presence of a high agglutinin titer in the serum. One might question whether this case should have been included, but because the clinical course was similar to that in Case 1, we consider inclusion justified, although the organism was not isolated.

The antigen for the agglutination tests was prepared from freshly isolated strains suspended in 0.5 per cent phenol in physiologic saline solution. In each case the serum gave a flocculent ("flagellar") type of agglutination. As would be expected by reason of common somatic antigens, O strains of typhoid bacilli were also agglutinated by these serums in high dilution.

Epidemiology

Data concerning the number of troops affected in this outbreak of *S. enteritidis* infection are unobtainable, because in most cases the symptoms were probably mild and because, in the exigencies of bitter jungle fighting, many men failed to report diarrheas and even fevers that were not incapacitating; nor were adequate diagnostic facilities available at the front.

Although the evidence is not conclusive, it seems likely that the majority of infections were contracted from the same source and at about the same time. All the cases presented above did not occur in the same company, but they occurred in the small Buna-Sanananda area of the jungle for varying periods during December, 1942, and January, 1943. For three days — that is, from December 25 to 27 — 5 of the 6 patients were there simultaneously. It seems reasonable to assume that infection took place at or about that time. To our knowledge no subsequent cases of infection with *S. enteritidis* occurred elsewhere as the campaign progressed in New Guinea.

Nor have we any definite evidence regarding the source of the outbreak. It appears unlikely that infection occurred from the ingestion of food products from infected animals — the usual source of Salmonella outbreaks — since the diet of the troops was limited entirely to C rations, which consisted of dried and tinned food processed in the United States. Infection may have originated from a carrier of the organism among Allied or enemy troops or from one of the native bearers. Rats have been known to harbor the organism,[12] and there were many rats in the area.

The infection was probably transmitted through contaminated drinking water. Water was obtained from the corpse-strewn, rat-infested swamps in which the troops fought. Boiling was rarely possible, and individual chlorination was at best haphazard. The epidemic may have been fly-borne, for flies were plentiful. Excreta were usually deposited where circumstances permitted.

Discussion

In a recent review of Salmonella infections, Bornstein[13] describes the following clinical syndromes resulting from human infection with these organisms:

> *Salmonella gastroenteritis.* The essential features are the abrupt onset of vomiting and nonbloody diarrhea eight to thirty-six hours after the ingestion of contaminated food or water. There may be slight fever for a few days, but there is usually prompt recovery.
>
> *Salmonella fever.* A typhoid-like course, leukopenia, splenomegaly, abdominal pain and occasionally vomiting and diarrhea occur. The disease is generally milder and less typical than that caused by *E. typhosa.* Blood cultures are positive early in the disease.
>
> *Salmonella septicemia.* Impressive invasion of the blood stream is usually present from the onset of a high remittent fever. Localization of the infection through hematogenous dissemination is likely and spares few structures. Bronchopneumonia, osteomyelitis, meningitis, pyarthrosis and endocarditis are not rare.

Bornstein stresses the point that on occasion any Salmonella may produce one of the syndromes listed above. The clinical course in the cases reported above was far different from that in the simple gastroenteritis usually produced by this organism. In 5 cases there was prolonged fever simulating that seen in infections caused by *E. typhosa*, an organism with which *S. enteritidis* shares common somatic antigens. In all cases there were prominent suppurative features such as are occasionally seen in infections with Group C Salmonella organisms, particularly *S. choleraesuis.*[14]

Lack of familiarity with the natural history of Salmonella septicemia and its sequelae led to delay in diagnosis in most of the cases. In none was the diagnosis made on admission to the hospital. In retrospect, however, survey of the clinical features brings out certain distinctive characteristics.

The 6 patients may be separated into two groups: those who developed a sustained nonmalarial fever and evidence of blood-stream invasion while in the combat area, where opportunity for this infection was present, and those who had no characteristic symptoms of Salmonella infection until suppurative lesions manifested themselves three to six months after the patient had left the combat area. This prolonged period of asymptomatic infection was the striking feature in the latter group of cases, but even in the first group the sometimes indolent character and always insidious development of suppurative lesions were noteworthy. In Case 1 five weeks had elapsed and the initial fever had abated before the appearance of subcutaneous swelling overlying

a costal cartilage indicated the presenting abscess. The patient in Case 2 had been convalescent for four weeks after nine weeks of fever, pneumonitis and urinary-tract infection when he developed excruciating pain in the back and a recurrence of fever that lasted for five weeks. X-ray examination ultimately revealed destructive changes in two lumbar vertebras. Case 3 illustrates an earlier appearance of symptoms referable to localized infection, but the abscess was long in developing to a conspicuous degree. This patient noted a tender area on the anterior aspect of the chest wall during his initial twelve-day fever. It was not until three months later that a suppurating mass appeared in the area and gave the first opportunity for correct diagnosis.

Cases 4 and 5, in the second group, closely resembled Case 2 except that the patients did not have a sufficiently prolonged initial fever to warrant hospitalization. As in Case 2 the subsequent onset of symptoms of localized Salmonella infection was accompanied by fever. In Case 4 the association of the fever with a normal white-cell count and pain in the left upper quadrant and shoulder led to a tentative diagnosis of malaria despite the absence of parasites in the blood smears. Antimalarial treatment was unavailing. It was not until an abscess presented and was drained that the diagnosis of Salmonella infection was established and its tendency to manifest itself in localized suppuration was recognized. Again, in Case 5, the backache was at first erroneously attributed to malaria without due consideration for the severity of the pain and with delay in obtaining x-ray evidence of osteomyelitis of the lumbar spine. Case 6 was unique in that the slow development of a testicular abscess was not associated with fever.

The propensity of the patients to develop recurrences of fever is noteworthy. Fever usually reappeared in association with the suppurative lesions. In Case 1 the blood culture was positive for *S. enteritidis* during the relapse. The second febrile episode in Cases 4 and 5 may well have represented recurrences of bacteremia also.

The likelihood of genitourinary-tract infection in the early stage of bacteremia is borne out by the presence of epididymitis in Cases 1 and 2, positive urine cultures for the organism in Cases 4 and 5 and the development of a testicular abscess in Case 6.

The localization of infection in the costal cartilage in 2 cases bears an interesting similarity to the behavior of other Salmonella infections. Ssokoloff[15] described 10 cases in which *S. choleraesuis* produced a costal chondritis. The cases occurred during the Russian typhoid-paratyphoid epidemic of 1919–1923 and were generally associated with a "paratyphoid relapse."

Various sulfonamides have been reported of value in the treatment of Salmonella infections. No definite conclusions, however, can be drawn regarding the efficacy of sulfonamide therapy in the cases presented above. Different drugs were administered in varying dosages for arbitrary periods during the infections. In only 1 case (Case 2) did a sulfonamide appear to exert no beneficial effect whatever.

In 4 cases a stool-carrier state developed. In each case the organism disappeared from the stool following sulfaguanidine in doses varying from 3 gm. every four hours to 3 gm. every eight hours, continued for several weeks. But this apparent success must be interpreted in light of the observation that convalescent Salmonella carrier states usually terminate spontaneously in a matter of weeks.[13]

Summary

An outbreak of infection caused by *Salmonella enteritidis* among troups in the Papuan campaign in New Guinea is reported.

In some cases the disease progressed far beyond the acute gastroenteritis usually associated with infections caused by this organism. Six cases seen in a general hospital with late manifestations of the infection are presented. In 5 the infection was associated with a condition similar to typhoid fever. All cases eventually developed focal suppuration.

The cases serve to illustrate the recent concept of the protean nature of Salmonella infections.

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FAMILIAL HEMORRHAGIC TELANGIECTASIA*

With a Note on the Use of Oxidized Cellulose Gauze as a Hemostatic Agent in Epistaxis

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THE occurrence of epistaxis in association with developmental anomalies of the blood vessels was first mentioned by Sutton[1] in 1864. Babington[2] described hereditary epistaxis in 1865. Thirty-one years later Rendu[3] reported the same condition in a patient with cutaneous angiomas. The classic monograph of Sir William Osler[4] in 1901 on a form of familial recurrent epistaxis associated with multiple telangiectases of the skin and mucous membranes did much to establish the syndrome as a clinical entity. Weber[5] presented an account of another case of this rare disorder in 1907. Today, the Rendu–Osler–Weber disease, often referred to as Osler's disease, is known as familial hemorrhagic telangiectasia.

Although there is reason to believe that this disease occurs much more frequently than the number of reported cases indicates, about 500 patients in more than a hundred families have been described in the literature up to the present time. The disease occurs equally in both sexes, and is transmitted as a simple dominant by both men and women. Wintrobe[6] states that families of the following stocks are affected in the order indicated: Anglo-German, Latin, Scandinavian and Jewish.

The cause of this morbid derangement of the capillaries is unknown, but the condition has been placed in the nondescript group of disorders often referred to as exhibiting degenerative stigmas. Teahan[7] has traced the disease in six generations of one family. Since severe bleeding does not begin until the fourth or fifth decade, it has been thought that an endocrine factor at least aggravates the bleeding tendency. The results of estrogenic therapy have not supported this belief. Arteriosclerosis and aging processes may contribute to the hemorrhagic proclivity, but even here the evidence is not too convincing. It is interesting to note that Singer and Wolfson[8] found increased capillary fragility as evidenced by a positive tourniquet test in their study. These authors link the disorder to hereditary familial vascular purpura. Wells[9] reported 2 cases of the disease with a prolonged bleeding time, in one of which the patient showed increased capillary fragility. As a result of these findings Wells believes that the disease also overlaps von Willebrand's[10] pseudohemophilia. Familial hemorrhagic telangiectasia, hereditary familial vascular purpura, and pseudohemophilia, together with familial epistaxis without telangiectasia, may stem from a common hereditary vascular dysplasia. With the present unsatisfactory classification of these diseases in mind, these disorders are reviewed in the light of newer physiologic and anatomic findings.

The telangiectases have been known to occur in almost every organ of the body. On the skin they appear as small violaceous spots 0.1 to 3.0 mm. in diameter. Spider telangiectases are sometimes visible on the face, and large vascular nevi covering the nose have been reported.[11] On the nasal mucosa the small reddish purple spots dot the septum and floor of the cavity. They may be seen on the tongue and oral mucosa. Lesions have been reported in the stomach on gastroscopic examination[12] and have been confused with ulcer, with which they may be associated. Telangiectasia of the lungs may be a more frequent cause of pulmonary hemorrhage than is ordinarily thought. Hematuria has been described by continental writers,[13] and it is well to inquire carefully about familial bleeding in cases of essential hematuria in patients over forty years of age. The lesions of the skin are not always permanent as has been stated in the literature. In the case reported below, the telangiectases were often absent at various examinations. Hepatomegaly, splenomegaly and increasing intolerance to blood transfusions of Type O have been reported by Fitz-Hugh.[14] The blood picture in cases of familial hemorrhagic telangiectasia is normal, except for the posthemorrhagic anemia that results from the repeated bleeding. The microscopical features of the disorder have often been commented on.[15, 16] The terminal vessels, capillaries and venules are dilated and thinned. Covered by a scanty layer of epithelium, these thinned and dilated vessels are either easily traumatized or else ruptured by some unknown intrinsic factor, with resultant bleeding. It can be seen, then, that the disease is inherently a capillary disorder. Hemorrhage is usually associated with lesions of the nasal mucosa.

The typical telangiectases may be found early in life, but they seldom cause serious hemorrhage until the patient reaches the fourth decade. Epistaxis then becomes increasingly troublesome and serious as age advances. Many patients have the lesions but not the bleeding tendency. This, together with atavism,[17] may explain, to some extent, the absence of the disease in some generations of a family. Repeated hemorrhage — usually epistaxis — in either sex at about the fourth decade or after, a positive

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family history of bleeding and the presence of telangiectases on the skin and mucous membranes, particularly the nasal mucosa, suggest the diagnosis of familial hemorrhagic telangiectasia. The typical blood dyscrasias are usually excluded by the presence of normal blood physiology.

The most serious complication of the disease is fatal hemorrhage. The mortality from hemorrhage per se is given as 3 to 6 per cent by various authors. Most of the patients with familial hemorrhagic telangiectasia harbor a secondary anemia from the repeated blood loss. It is surprising how well they adapt themselves to this posthemorrhagic state.

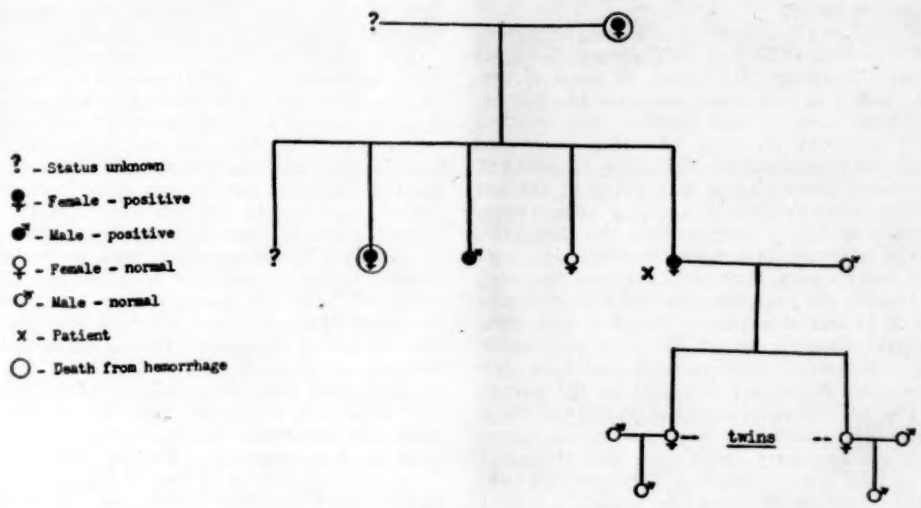

FIGURE 1.

Infarction of the lungs is apt to occur when bed rest is abused following hemorrhage. The alterations of the blood due to the anemia may be a contributing factor to the phlebothrombosis. It is conceivable that the anemia and prolonged hemorrhage in an arteriosclerotic heart may initiate an acute coronary insufficiency.

The prognosis, in the absence of complications and provided hemorrhage can be controlled, is good so far as life is concerned. The severe and at times intractable hemorrhage, together with the anemia, often either makes semi-invalids of these patients or causes them to live restricted lives. Because of the repeated epistaxis, they pay numerous visits to the emergency wards of hospitals.

The treatment of familial hemorrhagic telangiectasia consists essentially of the control of epistaxis of varying degrees of severity. The multitude of agents and measures used in arresting the hemorrhage attests to failure to find a satisfactory method of managing the victims of this disorder. According to recent reports rutin, one of the newer therapeutic agents for decreasing capillary fragility, although not a specific, may be of some help in controlling the hemorrhagic tendency.[18, 19] Endocrine preparations, as mentioned above, have given indifferent results. Some students of the disease think that snake venom helps to control the bleeding. Styptics and thromboplastin are of temporary value when applied locally in conjunction with pressure or a nasal pack. I have found a latex finger cot tied around the end of a catheter and inflated, to be a useful aid in maintaining hemostasis preparatory to the insertion of a nasal tampon. Radiation may induce a remission of one to three years, but it is reported to have caused destruction of the septum. No physician who has observed these patients after repeated and thorough cauterization can conscientiously say that he has been tremendously impressed by the results of this method of treatment. A measure of relief may be obtained by sclerosing of the vessels, but this requires a certain amount of skill that is outside the province of the average general practitioner. The fairly constant formation of new telangiectatic areas nullifies the effect of painstaking cauterization or sclerosis. Sooner or later one must rely on a tight vaseline-soaked gauze nasal pack. The patient complains of discomfort when this is inserted daily or every other day for weeks at a time, as is often necessary. The foul odor is obnoxious to the patient, to other members of the household and to the physician alike.

The case reported below illustrates the successful management of familial hemorrhagic telangiectasia and intractable epistaxis with a new hemostatic material, — oxidized cellulose gauze, — as described by Frantz and Lattes,[20] whose excellent article describes the preparation, action and uses of this latest addition to the list of hemostatic agents.

CASE REPORT

G. C., a 60-year-old housewife of Scottish-English extraction, was admitted to the hospital because of severe nosebleeds. Since childhood she had had epistaxis, which had always been controlled by ice and light nasal packings until about 5 years before admission, when the hemorrhages occurred

more frequently and became severer. She had had many hospital admissions for arrest of the bleeding. Four years before admission she had been treated with radium. During the next 2 or 3 years the bleeding was less severe and occurred at longer intervals. For the greater part of the previous 10 months the patient had had a firm nasal packing of vaseline gauze inserted in the right nostril. The packing was removed and reinserted daily or on alternate days. On some occasions during this period she was able to go about her duties for several days without the packing. Usually, a sudden severe nosebleed, initiated by a cough or sneeze during an attack of asthma, necessitated emergency treatment and a return to the nasal pack. During such episodes it was not unusual for her to lose 400 to 800 cc. of blood. At times she became so weak from hemorrhage that she was confined to bed for varying periods. While a patient at another hospital, she developed phlebothrombosis of both lower extremities and an infarct of the left lower lung. Bilateral superficial femoral-vein ligation was done, and she was discharged. She continued to have minor episodes of infarction after her return home.

The mother had died at the age of 52 of hemorrhage from the nose. A sister had died at 65 in a posthemorrhagic state following severe nasal bleeding. A brother, 63 years of age, had heart disease, and had had many hospital admissions, for nosebleeds. Three sons of this brother had reached adulthood without apparent bleeding. Another sister had died at the age of 21 of pneumonia following measles. A sister with hypertensive heart disease was living at the age of 68 and had no symptoms or signs of capillary hemorrhage. Each of twin daughters had a son; neither the daughters nor their sons showed telangiectases or any bleeding tendency.

The patient had had measles, mumps and whooping cough during childhood and for the past 20 years had had moderate to severe attacks of bronchial asthma. She had had three operations for frontal sinusitis about 30 years previously. At the age of 20, a bilateral oophorectomy had been performed. There were no symptoms referable to the gastrointestinal tract. The patient complained of slight exertional dyspnea and occasional attacks of pain across the upper chest. She had no genitourinary complaints and slept well when free from asthma and epistaxis. Menstruation had ceased following the operation 40 years previously.

Physical examination showed an obese woman who was bleeding rather profusely from the right nares through a firmly inserted nasal pack. Examination of the pharynx revealed postnasal hemorrhage. The nasal packing was removed, and a tight vaseline-soaked gauze tampon was inserted well into the cavity. The bleeding ceased, and the patient was given sedation and admitted to the hospital. The pulse was 92, and the blood pressure 60/50.

Examination of the blood disclosed a red-cell count of 3,700,000, with a hemoglobin of 69 per cent (9.9 gm. Sahli), and a white-cell count of 6400, with 43 per cent neutrophils, 50 per cent lymphocytes, 1 per cent eosinophils and 6 per cent monocytes. The clotting time was 4 minutes, and the bleeding time 1 minute. The platelet count was 290,000. The prothrombin time of the patient and a control was 23 seconds. The hematocrit was 34, the specific gravity of whole blood 1.045, and the mean cell diameter of the red cells 7.7 cubic microns. There was beginning clot retraction in 15 minutes, with completion in 3 hours. The resistance of the red cells to hypotonic saline solution was normal. The patient was Type I AB, and Rh+. There was no indication of increased capillary fragility by the tourniquet test. A blood Hinton test was negative. The urine was essentially normal except that the sediment contained many white cells in an uncatheterized specimen. A chest film showed slight blunting of the right costophrenic angle indicative of an old pleurisy and some lateral protraction of the lower left contour of the heart. An electrocardiogram showed small Q waves in Leads 1 and 2 and a low T wave in Lead 1. It was interpreted as being suggestive of myocardial damage.

Examination of the nose on the next day was unsatisfactory because of oozing, but a nose and throat consultant reported that the mucosa showed many telangiectatic areas and a moderate degree of atrophy. The telangiectases were more numerous and more marked on the right. A tiny, reddish-purple area was present on the tip of the tongue. A second lesion was seen on the ball of the index finger of the left hand. Several areas of telangiectases over the trunk, arms and thighs, seen on previous examinations, had disappeared. On the fifth hospital day the blood pressure was 120/90 and the pulse 80.

The nasal pack was removed daily and reinserted. On the 7th hospital day it was not replaced, in spite of slight oozing. Since the patient had had two severe transfusion reactions during a previous admission to another hospital and because it was feared that an increase in blood volume might initiate hemorrhage, she was discharged 21 days after admission with a red-cell count of 3,300,000 and a hemoglobin of 62 per cent (8.9 gm. Sahli).

Twenty-four days later she was readmitted with severe nasal hemorrhage. It was necessary to insert firm anterior and posterior nasal packs in the right nostril, as well as a light anterior pack in the left nostril. The patient was discharged on the following day with an anterior nasal pack of vaseline-soaked gauze. The red-cell count was 3,700,000, and the hemoglobin 58 per cent (8.3 gm. Sahli). The hemorrhage was well controlled. Ten days later she was seen in the Emergency Room with severe epistaxis. At that time a firm tampon was inserted in the right nostril. This was changed on alternate days in her home.

The fourth admission for severe epistaxis took place 18 days following the last treatment in the Emergency Room. Oozing from the right nares had been continuous for 5 or 6 days in spite of a firmly inserted nasal tampon. The red-cell count was 3,700,000, and the hemoglobin 64 per cent (9.1 gm. Sahli). The nasal packing was removed and reinserted. On the following day it was again removed. Bleeding had ceased, and it was not replaced. On the 3rd hospital day blood suddenly gushed from the right nostril following a cough, and the hemorrhage was controlled with difficulty. Several inches of oxidized cellulose gauze,* which had been obtained from the manufacturer at the suggestion of Dr. Roderick Macaulay, was inserted into the right nostril after the method of Houser.[21] After a lapse of 2 or 3 minutes the hemorrhage ceased. Two days later the resulting brittle material had been absorbed, and the bleeding began again. The nose was repacked, and the bleeding was almost immediately arrested. More of the material was used at this packing than previously. On the next day the gauze became granular and, within 24 hours, began to drop postnasally as tiny bits of a harmless gelatinous substance. Absorption and elimination were fairly complete in 7 days, and hemorrhage ensued. Prompt packing caused the bleeding to cease at once. The hemostatic material became loose in the nasal cavity and was removed 6 days after insertion. Inasmuch as epistaxis did not ensue, the pack was not reinserted. Eight days elapsed with only occasional episodes of minor oozing. This was readily controlled by the patient, but often stopped spontaneously. The patient was placed on 20 mg. of rutin 3 times a day, the immediate members of her family were given instructions on the insertion of the oxidized cellulose gauze, and she was discharged on the 26th hospital day. On subsequent office visits the amount of rutin was increased to 40 mg. 3 times a day. Because of nausea, it was necessary to reduce this dosage to a total daily maintenance dose of 100 mg. The hemorrhages, now easily controlled by oxidized cellulose gauze, have become less frequent and less severe since the institution of the rutin therapy. At present the patient is able to carry on all her normal activities, including household duties, with no difficulty.

Summary

The essential features of familial hemorrhagic telangiectasia (Rendu–Osler–Weber disease) are reviewed. The disease may be more closely related to other familial, hereditary hemorrhagic disorders than was formerly believed.

A case with intractable epistaxis is reported and discussed from the viewpoint of management with a new hemostatic product. Oxidized cellulose gauze should prove a useful addition to the therapeutic armamentarium for the control of epistaxis because

*The material used was a 1.2-cm. Hemo-Pak, manufactured by Johnson and Johnson, New Brunswick, New Jersey.

it is easily inserted, its hemostatic efficiency is high, it causes no discomfort to the patient, it is free from objectionable odor, and it is practically completely absorbed.

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RENAL INJURY FOLLOWING EXPOSURE TO CARBON TETRACHLORIDE*

Report of a Case

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MOST physicians associate carbon tetrachloride poisoning with serious liver damage and jaundice. This is not surprising, since knowledge of this substance stems from medical-school teaching, in which carbon tetrachloride was cited as an etiologic agent in toxic cirrhosis or acute atrophy of the liver and emphasis was placed on the risk of liver damage following the improper use of carbon tetrachloride as a vermifuge. The association of carbon tetrachloride with liver injury is also due in part to familiarity with its use as a hepatotoxic agent in animal experiments.[1–3] It is not generally recognized, however, that the inhalation of carbon tetrachloride by man frequently results in a clinical picture in which renal and pulmonary injury predominate and liver injury is not evident, although numerous authors have described such cases in more or less detail.[4–10] It appears that the syndrome of renal failure, accompanied by hypertension and severe azotemia induced by heavy exposure to carbon tetrachloride vapor, deserves additional emphasis in the general literature so that such cases may be recognized promptly and handled properly. The following case is therefore reported in detail.

G. L., a 51-year-old Italian laborer employed in a large, modern chemical plant in the Boston Metropolitan Area, was admitted to the hospital on June 14, 1946. He had been in good health all his life and was known to have had a normal blood pressure in 1945. According to his neighbors, he drank wine fairly steadily but seldom became drunk. On May 28 he and six other laborers were assigned the job of cleaning thick grease from the gears of a large mill prior to its being dismantled. They were at first given open buckets of naphtha and cloths with which to accomplish this task, but at 2:00 p.m. on May 29 the naphtha was replaced by carbon tetrachloride after an explosion-meter test indicated the presence of an explosive concentration of naphtha about them. The seven men then worked with open buckets of carbon tetrachloride in which they soaked their rags to dissolve the thick grease. The work was carried on in a large, open room with 31,044 square feet of floor space and with adequate general but no local ventilation. The men were instructed to leave the vicinity of the work and "get some fresh air" for about 5 minutes every ½ hour. Six of the men apparently did so to smoke. The patient, a nonsmoker and an unusually conscientious worker, did not take these rest periods but continued to work steadily. All seven men worked at this job from 2:00 to 4:30 p.m. on May 29. The plant was closed the next day, but on May 31 the same group worked from 8:00 a.m. to 4:30 p.m., except for a laborer who had been removed from the job about noon because he complained of "stomach ache and bleary vision." (This man's complaints cleared up on transfer to outdoor work and no subsequent illness developed.) On the following day the remaining six laborers again went to work with their buckets of carbon tetrachloride. The patient was removed from the job and assigned outdoor work about 2:00 p.m., after he had complained of dizziness and nausea. The remaining five men continued on the job, which they completed without incident or illness toward the end of the following week.

The patient felt worse instead of better after his transfer to outdoor work, and was forced to leave the plant early because of nausea and abdominal discomfort. At home that evening the nausea increased and was accompanied by frequent emesis. He complained of generalized crampy abdominal pain and severe occipital headache. Several chills occurred, although no fever was noticed by his wife. That night the patient developed a dry, hacking, nonproductive cough accompanied by pain in the lower chest and epigastrium. These complaints continued during the next 2 weeks, during which there were frequent bouts of vertigo, chills, extreme anorexia and nausea, as well as intermittent severe occipital headache. Vomiting occurred frequently, and on one occasion bright-red blood was noted in the vomitus. Considerable abdominal distention developed, although the bowels moved daily, the

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stools being normal in color and consistence. On several occasions there were complaints of intermittent dimming of vision, described as being "like a cloud over the sun." Blood clots were expelled from the nose frequently, although no frank nosebleeds were noted. At no time were there any clinical signs of icterus or any evidence of bile in the urine.

The cause of the illness apparently was not clear during this period, although the exposure to carbon tetrachloride had been brought to the attention of the family physician by the plant nurse. Diagnostic x-ray examinations, including a gallbladder series, gastrointestinal series and barium enema, were reported to be negative, although a small esophageal diverticulum was noted at the level of the seventh rib. The patient was referred to the hospital when his condition was becoming progressively worse, with increasing anorexia, vomiting, abdominal discomfort and lethargy.

Physical examination revealed a lethargic, somnolent, acutely ill patient. The breath was foul. No jaundice, cyanosis or petechiae were noted. The conjunctivas were pale, and the mucous membranes of the mouth were studded with purpuric spots. Examination of the chest revealed diminished expansion, but the lungs were clear throughout. The heart was slightly enlarged to the left, and the rate was regular and rapid, with a Grade I systolic murmur at the apex. The abdomen was soft and nontender. No organs or masses were palpable, and liver dullness was normal in extent. There was no evidence of free peritoneal fluid. The remainder of the physical examination was not remarkable.

The temperature was 98°F., the pulse 90, and the respirations 36. The blood pressure was 210/100.

Examination of the blood at the time of admission disclosed a hemoglobin of 15.1 gm. and a white-cell count of 11,500, with a fairly normal differential. The platelets appeared normal. The urine had a specific gravity of 1.010 and gave a + test for protein, and the sediment contained 40 to 50 red cells per high-power field. A rare cellular cast was noted. Blood chemical studies revealed the presence of a fairly severe nitrogen retention and moderate acidosis. The total protein, calcium, phosphorus and alkaline phosphatase were normal.

X-ray examination of the chest on the day after admission revealed a diffuse granular increase in the markings in both lung bases, most marked on the left, where there was a small amount of fluid in the costophrenic angle. These findings were interpreted as suggesting a resolving pneumonia at the bases. The x-ray film also disclosed slight cardiac enlargement. An electrocardiogram was normal.

The patient was given intravenous infusions of glucose, physiologic saline solution and sodium bicarbonate, as well as 10 gm. of methionine by mouth, and 5 cc. of crude liver extract intramuscularly each day. Lumbar puncture on the 2nd hospital day revealed no abnormalities. The patient remained restless and somewhat confused, and the nausea and headache continued during the first 3 hospital days. On the 4th day the patient began to feel better. The symptoms gradually lessened, and his condition slowly improved throughout the remainder of the hospital stay. On the 5th day, however, the temperature rose to 102°F. and the cough increased, although the lungs remained clear clinically. Intramuscular injections of 30,000 units of penicillin every 2 hours were administered from the 5th through 9th hospital day. The administration of penicillin was accompanied by a rapid fall in temperature to normal, disappearance of the cough and clearing of the x-ray picture. The blood pressure, which had been markedly elevated on admission, fell slowly to almost normal levels at the time of discharge. The blood urea nitrogen, blood pressure and other blood chemical changes during the hospital stay are presented in Table 1.

TABLE 1. *Pertinent Data during Hospital Stay.*

DATE	BLOOD PRESSURE	BODY WEIGHT	BLOOD UREA NITROGEN	CHLORIDE	CARBON DIOXIDE	THYMOL TURBIDITY	BROMSULFALEIN RETENTION (30 MIN.)	PHENOLSULFONEPHTHALEIN EXCRETION (2 HR.)	UREA CLEARANCE
	mm.Hg.	*kg.*	*mg./100 cc.*	*milliequiv./liter*	*milliequiv./liter*	*Maclagan units*	%	%	%
6/14/46	210/100	—	118	92	17.6	—	31	—	—
6/15/46	172/70	64.2	115	86	15.4	5	—	—	—
6/16/46	150/82	64.8	71	94	16.5	—	—	—	—
6/17/46	158/82	65.8	62	92	17.3	—	—	—	—
6/18/46	158/100	62.6	112	94	17.0	2	31	40	26
6/19/46	160/88	61.0	80	93	16.3	—	—	—	—
6/20/46	168/98	58.6	76	99	20.0	2	—	—	—
6/21/46	164/115	59.0	57	106	20.2	—	—	—	—
6/22/46	170/104	58.2	40	107	19.6	—	—	35	—
6/23/46	168/98	58.0	—	—	—	—	—	—	—
6/24/46	164/100	57.6	34	114	17.6	—	—	—	—
6/25/46	160/100	57.8	33	108	18.0	—	—	—	—
6/26/46	144/80	57.2	35	110	18.7	—	—	—	—
6/27/46	110/70	57.0	—	—	—	—	—	—	—
6/28/46	144/90	57.6	29	102	23.4	1	36	—	34
6/29/46	138/92	57.2	—	—	—	—	—	55	—
6/30/46	150/96	58.0	—	—	—	—	—	—	—
7/1/46	138/96	57.4	18	96	22.0	—	—	—	—
7/2/46	140/84	58.0	—	—	—	—	—	—	—
7/3/46	138/94	58.0	—	—	—	—	—	—	—

While the patient was in the hospital, special tests of liver and kidney function were performed. The thymol turbidity was never elevated above normal, although it dropped from a level of 5 Maclagan units[11] following admission to 1 unit at the time of discharge. The bromsulfalein test indicated a persistent increase in dye retention, but no elevation in serum bilirubin was present at any time. The urea clearance and phenolsulfonephthalein excretion were impaired throughout the hospital stay.

The patient was discharged from the hospital 20 days after admission. At that time he appeared well but still complained of frequent occipital headaches and generalized weakness. Six weeks after the exposure to carbon tetrachloride, he felt perfectly well and was able to return to work. At that time physical examination was not remarkable, and the liver and spleen were not palpable. The blood pressure was 136/82, and the nonprotein nitrogen 33 mg. per 100 cc.

This case illustrates several points in connection with poisoning following relatively brief exposure to carbon tetrachloride that deserve emphasis. The absence of any fire or explosion hazard has endowed carbon tetrachloride with a reputation as a safe solvent for general use that it does not deserve. In this case, carbon tetrachloride was substituted for naphtha to eliminate the explosion hazard accompanying the use of the inflammable solvent. It should have been evident that a toxic concentration of carbon tetrachloride would be encountered, since the explosion-meter test disclosed an explosive con-

centration of naphtha (this would be at least 1 per cent), and carbon tetrachloride is even more volatile. It is surprising that all the workers were not affected, for serious or even fatal poisoning may follow exposure to 0.1 to 0.5 per cent carbon tetrachloride.[12] There was undoubtedly considerable variation in the concentration actually breathed, however — the explosive naphtha concentrations were encountered near the buckets rather than at head level. Unfortunately, no carbon tetrachloride concentrations were determined.

Marked variation in susceptibility to poisoning by carbon tetrachloride has previously been noted.[12, 13] It is interesting that only two men of the seven exposed were affected and that only one was made seriously ill. It is quite possible, however, that careful examination and testing of the remaining men would have disclosed some evidences of kidney or liver injury.

It is impossible to state whether the therapy that the patient received after reaching the hospital had any pronounced effect on the course of the disease despite the diuresis and fall in blood urea nitrogen observed, since diuresis may be expected at about this time in the natural course of the disease. It appears probable, however, that the administration of fluids and electrolytes was helpful in promoting a return of kidney function. The effect of methionine on the clinical course is not clear; its action in protecting the livers of protein-depleted dogs from injury from chlorinated hydrocarbons has been amply demonstrated.[14, 15] Shaffer, Carpenter and Moses[3] have shown, however, that methionine is ineffective in preventing or correcting liver damage from carbon tetrachloride in dogs with an adequate protein reserve. The fact that the patient had eaten relatively little for the two weeks prior to admission made it appear desirable to give him an adequate protein intake. It was considered necessary, however, to maintain the protein intake at a relatively low level, adequate calories being supplied in the form of carbohydrate, to avoid an excessive accumulation of nitrogenous waste products in the body, and methionine was supplied in an effort to mitigate the undesirable effects on the already damaged liver of further protein depletion. Therapy in this case was directed primarily at the kidneys, since regeneration of the liver proceeds rapidly following acute poisoning by carbon tetrachloride and since liver damage in this case was not at any time sufficiently severe to cause clinical icterus. Conservative measures were adequate.

The multiplicity of action of carbon tetrachloride is well illustrated by this case. Definite evidences of pulmonary irritation and impaired liver function were noted, and the history suggested that gastrointestinal involvement was present during the first week of the illness. Reports in the literature indicate that carbon tetrachloride poisoning is characterized by pulmonary involvement[6] or acute abdominal symptoms,[16] as well as the more frequent renal or liver injury. Recently, carbon tetrachloride has been reported to induce the development of duodenal ulcer.[17]

Summary

The generally accepted but erroneous belief that acute carbon tetrachloride poisoning is usually associated with severe liver injury may lead to failure to establish a correct diagnosis in cases of carbon tetrachloride poisoning resulting from inhalation of its vapors.

A case of severe renal injury without clinical evidence of liver injury following brief but intense exposure to carbon tetrachloride vapor is presented in detail.

The clinical picture in this case was dominated by anorexia, lethargy, hypertension, azotemia and urinary findings suggestive of nephritis. Complete recovery, with a return of the blood pressure to normal, and disappearance of evidences of renal disease took place under conservative therapy.

The possibility that this syndrome occurs frequently following the inhalation of carbon tetrachloride is emphasized.

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THE DETECTION OF TUBERCLE BACILLI BY FLUORESCENCE MICROSCOPY

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THE method of fluorescent staining for the demonstration of tubercle bacilli in smears proposed in 1937 by Hagemann[1] offered a promising simplification of the rather cumbersome Ziehl–Neelsen technic. Many in this country have tried the procedure and have not been impressed with the results.[2] The objections are in some cases due to insufficient trial and in others to inadequate equipment. Better methods have now been developed, and it is the purpose of this paper to outline the technic and equipment and the results obtained therewith.

The tubercle bacillus does not fluoresce of its own accord but can be made to do so by staining with a fluorescent dye. Auramine O, readily available from several supply houses, was used in the studies described below. A saturated aqueous solution of this dye is filtered to remove the surplus undissolved particles. The filtrate is unstable but will retain its staining power as long as two weeks if kept in the refrigerator. Thinly spread, heat-fixed smears on new glass slides are stained for two minutes with this auramine solution at room temperature without the troublesome steaming required by the Ziehl–Neelsen method. The slides are then washed in water, decolorized with acid alcohol and again washed with water. They are then counterstained with a 1:1000 aqueous solution of potassium permanganate for thirty seconds, as recommended by Lee,[3] washed with water and allowed to dry in the air. The whole procedure requires only about three and a half minutes.

Light sources originally supplied for the purpose are not adequate. The present studies were done with a home-made lamp and filter described by Graham.[4, 5] The materials cost less than ten dollars. The essential parts are a 500-watt motion-picture projector bulb in a sheet metal housing, which also holds two 7.5-cm. double condensing lenses. It is necessary to delete from the lamp beam all but the blue light; this may be accomplished by the use of a liquid filter made as follows. An excess of ammonium hydroxide is added to a saturated aqueous solution of copper sulfate; this is placed in a rectangular museum jar and is diluted with water until the correct shade is obtained to give the results described below.

The wave length of the exciting and emitted light is further narrowed by placing in the ocular lens of the microscope a yellow glass filter equivalent to a Wratten K-2. This and the proper dilution of the aqueous filter will give a Nile-green background. This background for the microscopical field is chosen in preference to the black background usually advised. Against a green color, nonfluorescent elements on the slide are readily seen, and the focus can be maintained throughout the search for fluorescent particles. The green color minimizes eyestrain, to which some workers have objected. Another objection has been that a dark room is needed for examination of fluorescent-stained smears. When the green background is used it is only necessary to reduce the light in the examining room somewhat — for example, by drawing the shades nearest the microscope. We have found this most suitable for general use. Any standard monocular microscope with a 10x ocular and with 10x and 43x objectives may be used. No special quartz lenses are necessary. Nearly all oil-immersion lenses fluoresce and cannot be employed. The intensity of the fluorescence of the bacilli is not enough to allow the use of a binocular microscope.

The slides are first examined under low power and are searched systematically for yellow specks. The bacilli will, of course, be extremely small under this magnification, appearing only as minute rod-shaped flecks of yellow in the green field. They are, however, easily seen, and after a short period of practice, it is possible to search an entire slide under the low power in less than twenty minutes. As in the Ziehl–Neelsen stain, there are acid-fast fluorescent artifacts; thus, confirmation under higher power is necessary. With the high-dry lens it is possible to identify the tubercle bacillus more closely. It appears as a long, thin, irregularly stained rod that is pale whitish yellow. The bacillus usually has a slightly irregular outline.

Smears from a wide variety of sources have been examined by this method. These include exudates and caseous material from pleural cavities, meninges, bone and tendon sheaths, as well as sputum and gastric lavages. With few exceptions smears from these locations showed few artifacts, and these were easily differentiated from tubercle bacilli. Smears made from lymph nodes may be unsatisfactory because of the large number of artifacts. In sputum the number of artifacts is occasionally large enough to interfere with examination of the smear. Thus, in the hands of an inexperienced examiner, false positive-reactions may be reported. In the examination of seventy-six sputum specimens from healthy medical students, only two were found with so many artifacts that examination of the slide was unsatisfactory.

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In a series of 15 color-blind medical students, 10 found more tubercle bacilli in the examination of positive smears stained with the fluorescent method than they did in smears stained with the Ziehl–Neelsen technic.

Richards[6] reports that when the two stains are used in sequence on the same areas of the slide, more organisms appear with the fluorescent than with the Ziehl–Neelsen method.

Summary

The advantages of the fluorescent staining of the tubercle bacillus over the Ziehl–Neelsen technic are many. It requires only about three and a half minutes to stain a slide completely without the use of heat. Because of the use of lenses of lower power it is possible to examine a smear completely in less than twenty minutes — a point that has been made by Lind and Shaughnessy.[7] This method is considered more accurate than the Ziehl–Neelsen technic. The technic can be used safely for the screening of large numbers of sputums, the Ziehl–Neelsen method being restricted to the few specimens in which questionable fluorescent particles are encountered. Color-blind persons can identify the tubercle bacillus more readily with the fluorescent than with the Ziehl–Neelsen.

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MEDICAL PROGRESS

WAR WOUNDS OF THE ABDOMEN (Concluded)

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Liver. The liver is frequently involved in abdominal wounds, and almost always in right thoracoabdominal wounds. Consequently, x-ray films often show shell fragments within the liver shadow. Since these foreign bodies are well tolerated and their removal difficult, they are usually left in situ. This led to rather conservative therapy of liver wounds early in the war. It soon became evident that a more radical technic was required and that adequate drainage was necessary to avoid bile peritonitis, bile empyema or subdiaphragmatic abscesses. Although Betts[27] believes that a wound produced by a fragment 3 mm. or less in diameter, may be treated conservatively, the usual opinion is that any penetrating wound of the liver demands exploration, suture of any laceration of the diaphragm and the establishment of adequate subcostal drainage. This is due to the fact that the tiniest fragment may injure a large biliary radical.

The other major problem in the initial surgery of liver wounds is the control of hemorrhage. In the 829 patients studied by Madding, Lawrence and Kennedy,[2, 28] spontaneous hemostasis had occurred at the time of operation in 91 per cent. Various methods have been employed to control active bleeding. Fibrin foam or a hemostatic gelatin sponge should be ideal but was not available for this purpose. Large, deep sutures through the liver are often effective, but their use is hazardous, because they may initiate even more profuse bleeding. A tag of omentum may be placed in the defect. A detached portion of the rectus muscle may be of help. Large gauze packs have not been too satisfactory. They do not act as an adequate drain and, if left in place too long, form a large cavity that is slow to obliterate.

Madding advises the use of temporary gauze packs or a Penrose drain with gauze laid against the oozing surface. The drain should be started on the fourth or fifth day, and completely withdrawn by the tenth to the twelfth day. In only 1 case was grave postoperative hemorrhage encountered. Wounds near the hilus were most serious because of the proximity of other vital structures.

Gall bladder and bile ducts. These injuries are rare, and are nearly always associated with wounds of other viscera. Depending on the severity of the wound, an injured gall bladder may be treated either by suture and cholecystostomy or by cholecystectomy. Damaged ducts should be repaired. A successful two-stage repair was described by Park.[29]

Spleen. In World War I wounds of the spleen were treated by packing, with the result that mortality was high. Splenectomy was often performed, but the mortality was 100 per cent. In World War II the consensus was that splenectomy should be done whenever any treatment is warranted. The most interesting trend in the performance of splenectomy has been the widespread use of the transthoracic approach. Poole[2] found that the

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mortality in 159 cases removed by the transabdominal route was 29.5 per cent. The mortality in 171 cases of transthoracic splenectomy was 19.8 per cent. A transthoracic approach for strictly abdominal wounds, however, should not be made because of the possibility of fecal contamination of the pleura.

Kidneys. Wounds of the kidneys are treated either by packing or by nephrectomy. A conservative attitude is adopted whenever possible, nephrectomy being retained for severe damage to the vessels at the pedicle or to the renal pelvis, or for complete fragmentation of the organ. In the Second Auxiliary Surgical Group nephrectomy was required in 28.1 per cent of all cases; gauze packs were not favored. Postoperatively, urinary drainage generally continues for several days. A persistent urinary fistula, secondary hemorrhage and sepsis furnish the usual postoperative complications.

Ureter. In any wound in which it may have been damaged it is necessary to expose the ureter, since overlooked wounds lead to death from urinary extravasation. Tiny wounds can be sutured. High transections may be treated by a telescoping anastomosis. If the transection is low, the ureter may be reimplanted in the bladder. Kimbrough[30] advises suture of the injured ureter over a catheter and proximal diversion of the urinary stream.

Bladder. All patients suspected of bladder wounds should be catheterized preoperatively. Kimbrough[30] stresses the diagnostic value of this procedure and also advises digital rectal examination with the catheter in place.

Wounds are treated by suture and by suprapubic cystotomy. Urethral catheter drainage is not sufficient in itself to assure an empty bladder, and therefore must not be used to the exclusion of a suprapubic tube. It is also necessary to provide adequate drainage to the space of Retzius. The bladder is rarely involved alone, so that a careful search should be made for other visceral damage. Thus, Michels,[2] in 155 cases, found bowel damage in 88 per cent. There were no deaths when only the bladder was involved, and only 1 patient developed perivesicular infection.

Prostate and urethra. The value of primary repair of the membranous or prostatic urethra has been emphasized by Leadbetter.[31] He has described a method that can be carried out entirely through a suprapubic approach, and has obtained healing without stricture. The essentials of his technic comprise the passage of a urethral catheter, the accurate visual repair of the urethra, when possible, through the floor of the bladder and the anchoring of the dislocated prostate to its normal position in the perineum by deep stay sutures.

If this procedure cannot be carried out as a primary measure, a suprapubic cystotomy may be done, to be followed in a few days by a urethral repair. The importance of early repair is shown by the statistics of Conger,[32] who observed severe, nondilatable strictures in cases that were repaired six weeks after injury, whereas in those done soon after wounding the patients did well.

Pancreas. Wounds of the pancreas carry a high mortality chiefly because other viscera are injured at the same time. The usual treatment has been to establish drainage with a Penrose wick. The development of acute pancreatitis or skin irritation at the site of the drain frequently occurs if the patient survives.

Major Vascular Wounds

Patients with wounds of the aorta do not live to reach the surgical hospital. On the other hand, major wounds of the vena cava and the iliac, portal or superior mesenteric veins may be found on the operating table. These patients, according to Jarvis, Byers and Platt[14] show a characteristic clinical syndrome. Response to shock therapy is slight, but it is usually possible to raise the systolic pressure to 50 or 60. The pressure falls to 0 as soon as the peritoneal cavity is opened, and remains at that level until the bleeding is stopped.

If the wound can be controlled rapidly the patient may survive. Suture of a tangential wound or ligation of the vessel may be done. Packs or tangential clamps have been used in desperate cases, but are not recommended. Suture involves a greater hazard because of the possibility of embolism, so that ligation is preferred.

In 75 cases of major vascular injury observed at the Second Auxiliary Surgical Group the mortality was 73 per cent. No patient in the 8 cases in which the vena cava was ligated or sutured above the renal vessels survived. The major causes of death were hemorrhage (27 cases), anuria (12 cases) and pulmonary emboli (4 cases).

Swingle and Flynn,[2] discussing retroperitoneal hematomas, state that "the real significance [of such a hematoma] other than for the clinical signs which are indistinguishable from those of a viscus perforation lies in the fact that it may obscure injury to vital retroperitoneal structures." Therefore, if the position of the hematoma could indicate possible injury to the ureter, posterior aspect of colon, rectum, duodenum or bladder, these areas should be explored. Churchill[33] has pointed out that retroperitoneal hemorrhage is not a hazard per se unless the hemorrhage continues. In such an event the bleeding must be controlled.

Closure of the Incision

Insecure abdominal closure will lead to a high incidence of wound dehiscence, whereas if the closure is carried out by ordinary civilian methods there will be many serious infections. Thus, Jarvis, Byers and Platt[14] found that in the first 28 abdominal cases done by their surgical team there was dehiscence in 6 cases. Thereafter, they changed the

method of closure in a radical fashion, and in the next 100 cases had no disruptions. They recommend the following method. The peritoneum is closed with a running catgut suture. The posterior and anterior rectus sheaths are then closed with interrupted nonabsorbable sutures. This is further reinforced by numerous through-and-through sutures placed about 2 cm. lateral to the incision and about 1 cm. apart. A strip of vaseline-soaked gauze is placed between the skin edges down to the fascia. This gauze is removed in forty-eight hours. This same method is recommended by Churchill,[33] and others.

Certain methods of wound management were abandoned as experience increased. Laparotomies conducted through wounds of entrance and exit were found to be generally unsatisfactory. When colostomies were brought out through the main incision, the problems of infection and dehiscence were enhanced.

When a large part of the abdominal wall has been destroyed, tight closure will be impossible. Ogilvie[34] recommends the suture of a strip of vaseline-soaked canvas over the exposed bowel. This can be removed when granulations have formed over the bowel, and the hernia treated subsequently.

Evisceration

Patients with evisceration show an unusual degree of shock, and have a poor prognosis. Bradford, Battle and Pasachoff[35] found a mortality of 76.9 per cent in their cases with evisceration (omental eviscerations were not included). Childs[2, 36] found a 10 per cent incidence of evisceration in a series of 3154 cases of abdominal and thoracoabdominal wounds. The small bowel, omentum and colon were the usual organs involved, comprising 87 per cent of the group. The evisceration occurred more frequently at the wound of exit. The over-all mortality was 40.3 per cent — nearly twice as high as that in corresponding wounds without evisceration. If the colon alone had protruded the mortality was 57.5 per cent, and if the omentum alone, 37.2 per cent.

Thoracoabdominal Wounds

A full discussion of this subject is beyond the scope of this paper, but several important features of this group of wounds must be mentioned. Excellent analyses have been presented by Snyder,[37] DeBakey,[38] Wylie et al.[39] and Mason and Imes.[40] Shorter series are described by Welch and Tuhy,[41] Sanger[42] and Tuttle.[43] The features are as follows: any wound in which the diaphragm may have been traversed must be explored; with few exceptions, surgery of chest wounds should be done first in multiple wounds, thoracoabdominal wounds and combined intrathoracic and abdominal wounds; most thoracoabdominal wounds are best handled first by the thoracic approach, a celiotomy being performed only if the abdominal wounds cannot be cared for by the transdiaphragmatic route (the relative advantages of the various types of abdominal and thoracic incisions are described by Betts[27]); the incision, which should usually be made through the ninth and tenth rib bed or interspace, may be extended 2.5 to 5 cm. on to the abdominal wall if necessary[37] — and small accessory muscle-splitting incisions may be made for subdiaphragmatic drainage or exteriorization of colon, but extension onto the abdominal wall is not approved by some authorities, because the wound may break down[27, 39]; and the diaphragm must be sutured with nonabsorbable material, preferably in two layers.

A summary of the experience of the Second Auxiliary Surgical Group is presented in an excellent article by Wylie et al.[39] In 3532 patients with abdominal wounds, 25.5 per cent of cases were thoracoabdominal. The missiles had entered the abdomen from the thorax in 837 cases, and from the opposite direction in only 66. The right and left sides were equally involved. The authors discuss preoperative and postoperative treatment in detail, stressing the importance of accurate x-ray examination, the use of intercostal novocain block and postoperative bronchoscopic aspiration.

With right-sided wounds the liver was involved in 407 of 435 cases, followed in order, by the kidney, colon, stomach, small bowel, duodenum and gall bladder. On the left side, in 448 cases, the spleen was injured in 272, the stomach in 167, and the colon in 145. The liver, left kidney, small intestine and pancreas were involved with diminishing frequency. In 362 cases the whole operative procedure was carried out through the chest.

Mortality rates decreased progressively from 36.7 per cent in 1943 to 20 per cent in 1945. Wounds of five or more organs were uniformly fatal. In 234 fatal cases, the cause of death was shock in 130, peritonitis in 20, pneumonia in 17, renal failure in 15 and pulmonary emboli in 10.

Blast Injuries

Blast injuries of the abdomen were relatively infrequent in land warfare. Underwater explosions provided many small groups of cases that have been reported by various authors.

The mechanism of blast injury has been investigated by Greaves et al.[44] and by Webster and his associates.[45] They found that solid viscera are rarely affected. If the intestine is full of fluid it is also relatively immune, but if gas is present, there will be damage. Lesions were never found in animals in which the gastrointestinal tract was empty. Two types of lesion are found in fatal cases: complete perforation of the wall and hemorrhagic discoloration of the wall.

A typical sequence of symptoms is described by Webster et al.[45] as follows: a sensation of a tremendous blow on the abdomen at the time of the explosion; profuse vomiting, often of blood; bloody

diarrhea; severe abdominal pain; fever, the temperature averaging 102°F.; rigidity of the abdominal wall at one time or another; a white-cell count of 11,000 to 30,000; prolonged elevation of the sedimentation rate; and weight loss.

Operation is indicated for frank perforations soon after injury, for late perforations following hemorrhagic infarction and for drainage of abscesses.[46] The decision is often difficult because of associated pulmonary damage. It must be made within twelve hours, however, and doubtful cases explored.[45] In 7 cases operated on by Goligher, King and Simmons,[47] twenty perforations were found in each case, ranging from 1.0 to 3.7 cm. in diameter. The mortality in all cases is about 25 per cent.

Postoperative care. Essential features of the postoperative care include: replacement and maintenance of a normal blood volume, with constant check by copper sulfate studies of the hematocrit and serum protein — if blood volume determinations are available they will be of great value; the intravenous administration of adequate amounts of fluid, sugar, salt and, if available, protein; continuous nasogastric suction, not by means of Miller–Abbott tubes, which, in general, are too complicated for field use, but by a Levin tube, which is as effective if it is introduced before operation and maintained; accurate observation of the urine; special attention to the lungs to prevent pneumonia — intercostal block, tracheal or bronchoscopic aspiration may be necessary; chemotherapy; and gradual restoration of food intake as improvement occurs. It is of extreme importance that these cases are nontransportable for a period of ten to twelve days.

Reparative Surgery

This secondary surgery is performed in large hospitals in the Zone of Communications. In the Army general hospitals overseas the care of abdominal wounds was resolved into the following main categories: the management of colostomies; the drainage of residual abscesses and the care of septic wounds; and the treatment of intestinal obstruction. These topics are discussed below in order.

Management of Colostomies

Colcock[21] has stated that few colostomy patients escape without some complication, such as wound infection, wound separation, retraction of the colostomy, evisceration or the development of abdominal-wall, intra-abdominal, subphrenic or retroperitoneal abscesses. He suggests that practically all could be avoided by adequate mobilization of the colon. I have seen complete dissolution of the incision when the wound of entrance has been used as the exploratory incision and the colostomy brought out through it, serious abscesses after colostomy has been performed distal to the perforation and intraperitoneal retraction of the sigmoid colostomy when mobilization has not been sufficient. With increasing experience, these errors in initial surgery became less numerous.

Horsley and Michaux[48] observed the results in 111 cases in a general hospital in Italy, in which the colostomy closed in 40 cases and in which new colostomies were required in 5 because of the complications listed above. Whether or not a colostomy was to be closed was dictated to some extent by transportation facilities. The general rule was to evacuate the patient to the Zone of the Interior for closure if he was debilitated or had other severe injuries. If closure was to be done, the usual time was six weeks after injury. The procedure should not be attempted in the presence of wound sepsis or if peritonitis has existed within six to eight weeks, nor should it be done until all plastic surgery on the lower bowel, anal sphincter, urinary bladder or perineum has been completed.

It was found that a few minor perforations can be closed and the loop exteriorized — the perforations will heal, and the loop will then retract within the peritoneal cavity. Since all types of colostomies tend to retract, a glass rod should always be used with loop colostomies, and the bowel should be opened in the long axis on the oral side of the rod.

There was no mortality following closure, and fecal drainage occurred in only 1 case. The bowel could usually be closed with transverse sutures. In a few cases resection and end-to-end anastomosis were necessary. The bowel was always placed within the peritoneal cavity.

Gregg and Moseley[49] believe that digital examinations of the stoma will determine the best type of repair. With a loop colostomy, pressure with the finger will invaginate the posterior wall of the bowel into the peritoneal cavity. To close it, the colostomy is freed and turned in with two layers of transverse sutures. If a long, thin spur is present, it can be cut with crushing clamps. Closure is effected in the same fashion after tension on the bowel has been relieved by partial opening of the peritoneum. A thick spur indicates either a mesenteric artery from a rotated loop of colon or a loop of small bowel. In this event the peritoneum must be opened widely. If there is a constricted or retracted colostomy, plastic repair is done at the site of the stricture, which is opened longitudinally and closed transversely. The authors fear resection with end-to-end anastomosis — an apprehension that is unfounded in view of later reports.

Drainage of Residual Abscesses and Care of Septic Wounds

Wound care does not differ from that encountered in civilian practice. A conservative attitude may properly be taken so far as residual abscesses are concerned. Ogilvie[34, 50–52] has observed that practically all except subphrenic and pelvic abscesses tend to burrow to the surface, discharging spontaneously through the wound or incision. In my experience

many cases of subdiaphragmatic infections have subsided under adequate chemotherapy, and operation need not be considered urgent unless an undrained collection of bile is suspected. Pelvic abscesses can be drained easily through the rectum as soon as they become fluctuant. It is not advisable to wait for spontaneous rupture, since this may be delayed for a long period.

Treatment of Intestinal Obstruction

Obstruction of the small bowel is frequent after war wounds, probably because of the extreme trauma, hemorrhage and infection. This complication may appear at any time in the early convalescence or thereafter. Conservative therapy is unlikely to be successful except soon after the initial laparotomy, when the adhesions are still of a plastic type. Later, laparotomy will be necessary. Many adhesions are usually found, and it is generally unwise to attempt to free them all; only the obstruction can be relieved in most cases.[53] Enteroanastomosis may be necessary if the lumen of the bowel has been compromised by previous obstruction.

The late care of thoracoabdominal wounds in an overseas general hospital was discussed by Fox.[54] Of 270 patients only 43 per cent required further operations, 36 per cent secondary closure of wounds, 11 per cent thoracotomy for empyema, 5.2 per cent exploration of the subphrenic region, 4.4 per cent colostomy closure and 1.8 per cent decortication. The mortality was 2.6 per cent. Complications consisted chiefly of empyema and subphrenic abscesses.

Reconstructive Surgery

Reconstructive surgery is performed in the hospitals of the Zone of the Interior. As in the overseas general hospitals the main problem is that of colostomy closure. In addition, wounds of the rectum are closed, incisional hernias are repaired, urethral strictures may need operative intervention, occasional cases of intestinal obstruction require operation, and some foreign bodies are removed.

Colostomy Closure

Many papers have appeared on the subject of colostomy closures. At present all the cases in which closure has been done in the general hospitals of the Army are being collected by Poer[55] and will be published shortly. It is his impression that intraperitoneal end-to-end anastomosis should be performed. He has found a high degree of immunity to infection in these patients and has been unable to prove that preoperative or postoperative chemotherapy has improved the results. There were only 17 deaths in over 2000 cases.

Several other surgeons have presented smaller series but have reached essentially the same conclusions. Roettig, Glasser and Barney[56] advise the intraperitoneal closure because there may be unpleasant sensations when the bowel is incarcerated on straining or defecation, because ventral hernia is frequent after extraperitoneal closure, and because an extraperitoneal closure offers a good site for internal herniation and strangulation of small bowel. Foisie[57] also advocates an intraperitoneal closure. He was able to prepare most of his cases by crushing the spur.

Keene[58, 59] notes that if two colonic stomas are in such proximity that the same dressing covers both, feces will progress from one to the other. He states that a patient with a colostomy invariably builds up a fecal impaction in the distal loop while being evacuated to the United States. He believes that resection and open end-to-end anastomosis are so satisfactory that, when a proximal colostomy is made for a wound in the distal colon, the colon should be completely transected and the two stomas placed at least 6 cm. apart.

Saunders and Halperin[60] list the most frequent problems encountered in colostomy closure as subcutaneous herniation of the bowel, complete absence of a spur, interposed foreign bowel or mesentery between colostomy limbs, varying degrees of rotation of limbs, secondary perforation or fistulas, inflammatory or granulomatous masses and musculofascial defects in the abdominal wall. They believe that the anatomic repair of these defects requires an intraperitoneal operation. They favor and describe the Pauchet closure.

Hamilton[61] found that extraperitoneal closure was associated with a much higher incidence of complications than intraperitoneal. Recurrent fecal fistula and intestinal obstruction were frequent after extraperitoneal closures.

Advocates of extraperitoneal closures include Pilcher and Nadeau.[62] Shallow, Eger and Tourish,[63] from civilian experience, have described a method of closure that falls in the same group.

A critical survey of these various reports suggests the following conclusions. After proper preparation, the mortality following any type of closure is extremely low. Plastic and extraperitoneal closures occasionally develop temporary fecal fistulas or intestinal obstruction. Postoperative barium enemas will demonstrate a surprising amount of stenosis in many cases, even though the patients are clinically free of symptoms. The complications can be avoided by resection of the involved bowel, an open end-to-end anastomosis and secondary closure of the abdominal wound. This is therefore the preferable method.

In colostomy closure various other problems arise. One of the most important is the selection of the proper time for operation. All agree that the other operative procedures in the pelvis must first be completed, and that the patient must be in a good state of nutrition. Preferably, he should be within 10 pounds of his normal weight.

The exact method of preparation of the bowel for closure has varied considerably. Usually, meticulous mechanical cleansing of the bowel was associated with several days of preoperative chemotherapy in the form of sulfasuxidine, sulfathalidine or sulfaguanidine. Preoperative barium studies of all the distal and proximal bowel, as well as x-ray visualization of any fistulas present, are important.

Closure of Rectal Wounds

Hamilton,[61] describing the operative technic, states that these wounds are serious, because there is usually much scar tissue in the rectal wall and often a stricture or abscess as well. A completely defunctioning colostomy is essential. A generous incision should be made with removal of the coccyx and the fifth and fourth sacral segments if necessary. The rectal wall must be freed widely. Stenosis may be corrected by a longitudinal incision with transverse closure well away from the fistula. The fistula should be closed with two or three layers of sutures. Any associated foreign body that contributes to persistent sepsis is removed. The incision is allowed to heal by granulation.

Roettig, Glasser and Barney[56] state there are three important steps in closure of rectal perforations: adequate exposure, with removal of the coccyx and as much of the sacrum as necessary; as wide mobilization of the rectum as possible, both laterally and in front of the sacrum; and interposition of some fat or muscle tissue between the portion of the rectum containing transverse closure and the sacrum before the skin is closed. The wound is closed without drainage.

Laceration of Anal Sphincter

In such cases a colostomy is essential, according to Roettig, Glasser and Barney.[56] The sphincter is mobilized through a semicircular incision 3 cm. from the mucocutaneous margin. If closure is still impossible, the defect should be reduced as much as feasible. A second stage is carried out several weeks later after sphincter-control exercises and daily dilatation. Sphincter action and control must be tested before the colostomy is closed.

Intestinal Obstruction

Barney, Roettig and Jones[64] observed that in the last year in the Rhoads General Hospital, mechanical obstruction was found in a ratio of 1:18.5 cases. The incidence in the small bowel was three and a half times that in the large bowel. In the former all types of obstruction were found, whereas in the colon the most frequent cause was a small lumen following colostomy closure.

In the experience of these authors the incidence of strangulation of the small intestine or marked interference with blood supply was far greater in war wounds than the usual 10 per cent figure in civilian practice. They therefore advocate early laparotomy rather than the use of the Miller–Abbott tube. If the obstruction is in the colon, an attempt is made to delay operation long enough to give the patient an adequate amount of the sulfonamides. Thereafter, a resection and end-to-end anastomosis are done.

Removal of Foreign Bodies

Intraperitoneal foreign bodies are preferably removed at the time of initial surgery. Large shell fragments that have not been recovered may be removed in the Zone of the Interior. Those that contribute to persistent fecal or urinary fistulas, osteomyelitis or continued purulent discharge from a wound must be taken out. In addition, many that are in close relation to large vessels or to the hollow viscera should be removed. Those buried in the retroperitoneal musculature and in the liver usually produce no symptoms and may be left in place.

Repair of Hernia

No special problems are presented except that fascial repairs of hernias are frequently necessary.

Late Urinary Problems

Kimbrough[30] found that of the urogenital injuries seen in the general hospitals in this country, the kidneys had been wounded in 14.0 per cent, the ureter in 3.4 per cent, the bladder in 14.5 per cent, and the external genitalia in 68.1 per cent of patients. Nephrectomy had been performed in only 24 per cent of patients with kidney wounds. Prather[45] observed that nephrectomy was necessary in 2 of 3 cases of ureteral fistula evacuated to the Zone of the Interior.

The importance of early repair of the urethra[32] and the difficulty attending late attempts have been stressed by Conger.[32] Stricture is frequent after late repair, and dilatation is often impossible.

Rectovesicocutaneous fistulas are the most difficult late sequelae of bladder wounds to treat. Roettig, Glasser and Barney[56] state that the fistulas usually heal spontaneously if colostomy, suprapubic cystostomy and inlying urethral catheters are used.

Cystitis and epididymitis were also found to be frequent complications after bladder wounds.

* * *

In conclusion it might be appropriate to list several of the unsolved problems of abdominal surgery in warfare. The first and the most important is an accurate appraisal of the role of chemotherapy, both in the prophylaxis and in the treatment of peritonitis and other types of sepsis.

The prophylaxis of peritonitis has not yet been possible. Early in the war many soldiers took sulfonamide tablets by mouth immediately after they were wounded. It is obvious that the sulfonamides were useless in this fashion. The introduction

of streptomycin and of the relatively nonabsorbable sulfonamides, sulfasuxidine and sulfathaladine, however, offers a method to reduce significantly the number of virulent organisms in the gastrointestinal tract. It may be possible to develop a technic for the oral administration of these drugs for a few days before battle that would be valuable.

So far as the therapeutic administration of the sulfonamides and penicillin is concerned, it is impossible to assess their value satisfactorily. The variability of the types of wounds, the absence of any adequate control series and the omission of details of therapy in many records indicate that opinions rather than facts have been recorded. Furthermore, compared with the dosage that is employed today, penicillin was not available in sufficient quantities to influence the course of an established peritonitis.

Lyons[66, 67] emphasized the fact that adequate excision of devitalized tissue is much more important than the bacterial flora of the wound. He further stated as follows:

> Sulfonamide therapy has been shown to be adequate for the wound in danger only of hemolytic streptococci. Penicillin is the drug of choice for all other wounds subject to invasive infections. No virtue is attached to combinations of penicillin, and a sulfonamide compound as the treatment of infected wounds.

He concludes that local chemotherapy is unnecessary and undesirable and that penicillin administered parenterally is the chemotherapeutic agent of choice.

Imes,[68] discussing traumatic surgery of the abdomen, believed that the sulfonamides and penicillin were about equally effective in the treatment and prevention of peritonitis and that there was little doubt that chemotherapy played a significant role in the lower incidence of peritoneal infections following abdominal injuries. Drye[2] agreed that penicillin and the sulfonamides were important, but found it impossible to assess them accurately. He considered the mortality significantly lower, however, in the series treated with penicillin than in that in which sulfonamides were employed.

A second problem is concerned with the resuscitation of the wounded. Why is it that many patients, especially those with abdominal wounds, cannot be brought out of shock? Despite blood replacement and adequate surgery the blood pressure remains low, and death occurs in twenty-four to forty-eight hours. It is generally believed that overwhelming infection is present, but further clarification is needed.

A third problem is that of the so-called "multiplicity factor." Why is it that a man with five wounds of the small intestine has an excellent chance of survival, whereas a single wound of five viscera is almost uniformly fatal?

Moreover, the technical management of wounds of the colon demands further consideration. When one realizes that practically all the abdominal surgery in general hospitals in the Zone of the Interior is concerned with the management of colostomies, it can be appreciated that any safe method whereby the convalescent period could be shortened would be of value. Thus, Imes[69] has observed that "the contention of those who hold that all wounds of the colon should be exteriorized because of its poor healing tendency and greater than apparent tissue damage from shell fragments is not supported by our experience." In particular, then, is there a place for primary closure of wounds of the colon, or is this such an unsafe procedure in the hands of the ordinary surgeon that it should not be countenanced? Also, what is the best method of management of severe wounds of the right portion of the colon?

Finally, in common with other extensive wounds, what is the explanation of postoperative renal failure? This is one of the most important causes of death in patients who survive the period of shock.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 33321

Presentation of Case

First admission. A twenty-nine-year-old Jewish housewife was admitted to the hospital because of diarrhea.

The patient's illness dated from an automobile accident nine years previously, which was followed by a nervous breakdown. At that time she was supposed to have had a spine injury, which required six months' treatment, and during the convalescence she developed diarrhea (six to fifteen movements a day), which continued more or less constantly until admission to the hospital. There was no blood or mucus but merely watery diarrhea. Treatment by many physicians in several parts of the country gave no relief, and four years before entry she was explored at an outside hospital. Dilated portions of small bowel, which were about the size of the large bowel, with other areas of constriction and marked thickening of the wall, were noted. There was marked fusion of the mesenteric lymph nodes, with the formation of large masses. The mesentery was extremely friable and bled readily. The diagnosis was thought to be tuberculosis of the small bowel extending from the ligament of Treitz to within 75 cm. of the ileocecal valve. The patient improved markedly following laparotomy, and three weeks later she had the first formed stool in a year. She spent about six months in Arizona, felt much better and gained about 30 pounds. Two years later, however, the diarrhea and emotional upsets returned, and the following year she was studied at another hospital, where tuberculosis was supposedly ruled out by x-ray examination and skin tests. A diagnosis of ileitis was made at that time. She continued to have six to fifteen movements a day, remained somewhat high-strung, tired easily, and lost about 20 pounds.

Physical examination revealed a small, thin, poorly nourished woman with a high diaphragm and tympany over the normal liver dullness. On the left side of the abdomen a large mass was palpated and percussed 8 cm. below the costal margin. No shifting dullness or other evidence of fluid was found. The abdomen was slightly distended and felt doughy.

The examination of the blood and urine was negative. The stools were liquid and guaiac negative. A barium enema required nearly three times the usual quantity for filling. The colon was grossly

dilated and atonic. The ileum would not fill. There was slight deformity in the region of the ileocecal valve, but the mucosa was apparently intact. The hepatic flexure rose unusually high, whereas the splenic flexure was displaced downward; the entire abdomen appeared more dense than usual, possibly due to ascites. There were no gas-filled loops of small bowel. A gastrointestinal series revealed the stomach to be markedly displaced to the right and upward; there was a definite delay in emptying of the jejunum, with marked distortion. There was one long loop on the left side, about twice the normal size, that remained filled until the six-hour examination. After four hours the terminal ileum was fairly well filled and appeared small and slightly irregular; with the patient upright, fluid levels formed in the dilated small bowel but no gas was present. Examination of the chest was negative except for the unusually high diaphragm. She was discharged on the fourth day.

Second admission (one and a half years later). The patient was fairly well until seven months before entry, when she developed vomiting attacks that increased in severity. There appeared to be no exciting cause, and at the time of admission they were occurring every forty-eight to seventy-two hours, always preceded by nausea and occurring during the day. Despite this she had gained weight and felt much better than she had two years previously.

Physical examination revealed clubbing of the fingers and a doughy, tender abdomen. The spleen was palpable two fingerbreadths below the left costal margin.

Routine laboratory data were negative, and a barium enema revealed a deformity of the ileocecal valve and a dilated terminal ileum. On the second day a laparotomy was performed. At the operation a loop of small bowel was found glued to the abdominal wall; the intestine was greatly thickened, as was the mesentery of the small bowel, which was quite firm. There was interadherence of loops of small bowel and the mesenteries, and an enormous loop of jejunum could be elevated into the wound. A short circuit was performed between the distended, thickened jejunum and a piece of comparatively healthy, normal-sized small bowel. It was estimated, however, that at least half the small bowel was involved and possibly more. Areas of bowel that were obviously previously diseased could be seen in all quadrants of the abdomen. A biopsy of jejunum showed chronic inflammatory changes of a nonspecific nature.

The patient improved and was discharged about one month after admission.

Third admission (six and a half years later). The patient returned for evaluation of a therapeutic abortion. She was two and a half months pregnant. Because the patient was free from symptoms, abortion was not performed.

Fourth admission (three years later). The patient had been delivered of an infant by cesarean section two and a half years previously and subsequently developed sudden marked abdominal distention, with rupture of the operative sutures. Following this the distention subsided spontaneously. Two and a half months before admission she had noted that her abdomen seemed unusually swollen, and it had remained so. There were no other symptoms.

Physical examination revealed only slight distention and tenderness of the upper abdomen and pitting edema of the lower edge, more so on the left, than on the right, with slight tenderness on the left.

Laboratory data, including total protein and nonprotein nitrogen levels, Congo red test and prothrombin time, were negative. A cephalin flocculation test was + in twenty-four hours and ++ in forty-eight hours. X-ray studies revealed clear lung fields and a high diaphragm, especially on the left. The heart and mediastinum showed a slight shift to the right. Diaphragmatic motion was active and equal. There was a gas bubble between the anterior portion of the right leaf of the diaphragm and the liver, with a fluid level beneath it, which was interpreted as bowel between the liver and diaphragm. The upper half of the abdomen showed a homogeneous increased density that extended below the right iliac crest and was inseparable from the liver shadow. A plain film of the abdomen failed to show bowel in the upper right abdomen and midabdomen, but no definite liver shadow was seen. Upright films confirmed the presence of an air bubble in a confined area beneath the right leaf of the diaphragm, possibly air in an unusually high stomach.

Some observers thought they could feel a rather soft, possibly cystic mass in the upper abdomen, which on one occasion was said to be ballotable to the left flank from the right upper quadrant.

A gastrointestinal series and barium enema one week after admission revealed the stomach to be markedly displaced to the right and slightly forward by a large mass occupying the left upper quadrant. The mass appeared somewhat lobulated. In addition the stomach displaced the duodenum and small intestine downward. There was a small area of radiolucency, resembling fat, within the mass. A normal spleen was not visualized as in the previous films. The liver was small. A barium enema revealed an extrinsic soft-tissue mass displacing the transverse colon from above and posteriorly.

An exploration was done on the sixteenth hospital day.

Differential Diagnosis

Dr. Alfred Kranes: The remission of symptoms following a simple exploratory laparotomy seems extraordinary and raises considerable doubt regarding the diagnosis of tuberculosis of the small bowel.

As you might well imagine, this has been for me an extremely confusing problem and on first reading over the abstract I was completely bewildered. As I went over it more carefully it seemed to me that the patient's illness might be divided into two phases. The first, beginning at the age of twenty and ending at thirty, following the enterojejunostomy for obstruction, was characterized by symptoms resulting from the diseased small bowel. The second phase dated from thirty to the time of admission, when she was forty. According to the record, during the last ten years she was completely asymptomatic. Is that a fair assumption to make?

Dr. Daniel S. Ellis: Yes; after the operation at this hospital she was in perfectly good health.

Dr. Kranes: We have therefore to consider two questions. What was the nature of the small-bowel lesion that caused the original symptoms? Secondly, what was the nature of this mass in the left upper quadrant that brought her to the hospital at the age of forty? Is it fair to ask whether this patient survived the operation or came to autopsy? The reason I ask, is that time is short and I do not want to waste too much time on the small-bowel lesion.

Dr. Tracy B. Mallory: She survived the operation.

Dr. Kranes: If that is the case, it leads me to believe that they do not know any more about the disease in the small bowel than has already been described in the previous operative note and in the record. If that assumption is correct, I can probably speak freely about the probable nature of the small-bowel disease. It seems to me that the likeliest explanation for all the small-bowel symptoms is the diagnosis that was subsequently made, namely, regional enteritis. That diagnosis explains the history of this patient's illness and the x-ray findings, as well as the operative findings, more satisfactorily than anything else I can think of. The one thing that disturbs me greatly about the history of this illness is the fact that no pain was mentioned during the early part of the disease. That is unusual in any extensive lesion of the small bowel. Is it true that this patient never had any pain?

Dr. Allen: She had pain associated with nausea and vomiting before the first operation, the one done at another hospital.

Dr. Kranes: The original description of the bowel, as well as that of the mesentery and the large lymph nodes, is quite characteristic of regional enteritis, particularly the enlarged nodes. Some surgeons advocate removal of such lymph nodes, since it has been claimed that they are the reservoir of residual infection and predispose to recurrence. The disease has been experimentally produced, or a reasonable facsimile of it, by injecting sclerosing substances into the mesenteric lymphatic vessels. The histologic picture in animals is almost indistinguishable from that in human cases. Furthermore, the operative findings at the second laparotomy are quite in keeping with the diagnosis of regional enteritis. It is characteristic for inflammatory changes to be produced between loops of bowel and for fistulous tracts to form eventually. There were none in this patient. There is nothing in the history or symptoms or operative findings that contradicts the diagnosis of regional enteritis.

So far as tuberculosis goes, I think that is most unlikely, since ulcerative tuberculosis of the small bowel is usually a terminal event in advanced pulmonary tuberculosis. I also believe that the course of the disease is strongly against tuberculosis.

I shall leave that for a moment and go on to the mass in the left upper quadrant. What was its nature? I am afraid that I shall need quite a bit of help from the X-ray Department. I must confess that this description is exceedingly confusing. There seems to be an implication of two masses, one on the right side that extends to the right iliac region without any evidence of bowel in that region, and another on the left side. I was allowed to look at these films yesterday.

Dr. Richard Schatzki: I shall show you the outline of this mass; there was only one.

Dr. Kranes: The other thing that confuses me is the statement that a normal spleen was not visualized, as in the previous films. That to me is an important statement, because if a normal spleen was visualized on previous films, the diagnosis that has occurred to me must be completely discarded.

Dr. Ellis: There is only one mention of the spleen in all the films taken over a period of fifteen years.

Dr. Schatzki: No shadow of the spleen was visualized, unless one calls this peculiar mass the spleen.

Dr. Ellis: In the original examination Dr. Holmes described the spleen, which I am sure is the same mass that subsequently increased in size.

Dr. Schatzki: The original film was taken in 1936, and the mass at that time displaced the stomach to the right. In the next ten years it became eight times as large, displacing the stomach to the right and slightly forward and the colon downward.

Dr. Kranes: How about the small bowel?

Dr. Schatzki: There is nothing that can be added to the report.

Dr. Kranes: This mass is much larger than it was originally. What interests me is why it was not found at exploration. The operative note said nothing regarding it. I should have expected that a mass of that size would have been described, but perhaps the emergency of the intestinal obstruction and the extensive disease in the small bowel prevented extensive exploration within the abdomen.

Dr. Schatzki, was this mass separate from the left kidney?

Dr. Schatzki: Yes.

Dr. Kranes: In other words, it was a gradually increasing epigastric mass, probably chiefly in the left upper quadrant, completely asymptomatic and unattached to the stomach, to the kidney and probably to the adrenal gland. That leaves us little else to consider.

One point to be decided is whether or not this mass was in any way related to the previous disease of the small bowel. It is difficult for me to connect the small-bowel disease with the mass. Although it is true that regional enteritis not infrequently perforates and produces localized abscesses, it is impossible for me to believe that an abscess of this size could have been present for ten years without discomfort, fever or something in the way of symptoms. Furthermore, it is a most unusual site for an abscess. Finally, abscesses rarely attain the size described here. So I think I shall discard any relation between this mass and the previous small-bowel disease.

When one has multiple lesions and extensive disease within the abdomen, particularly a large mass in the left upper quadrant, the possibility of lymphoma comes to mind. Could the small-bowel disease have been lymphoma, and could the remissions have been due to the number of x-ray examinations she had had for many years? I hardly think that diagnostic x-ray doses could have produced this type of remission. The finding of large mesenteric nodes at the first operation is rather suggestive, but if she did have lymphoma, she must have cured herself spontaneously and I do not believe one can consider it seriously.

The next question to decide is whether the mass was solid or cystic. It seems to me that solid masses in this area and of this duration should have caused more in the way of symptoms. Furthermore, a large solid mass in this region should have been readily palpable. I am much more in favor of a cystic mass. The only cystic mass with which I am familiar in the left upper quadrant is a cyst of the spleen. That is the first thing that occurred to me, but as I studied the case more carefully, I hesitated to suggest it as a possibility because the condition is so rare. Yet I can think of no other explanation that fits all the findings in this case any better than a large cyst of the spleen. Actually, this patient had the proper background for such a diagnosis. Most of the cases described, of which there are not many, occurred in young women, and this started before the age of twenty-nine. A large proportion of them have a history of preceding trauma, which was present here. Most of these cysts, if that is what this is, contain old, brown, coagulated fluid, probably the result of the original hematoma.

In thinking of cystic diseases in this area, one also has to consider a dermoid cyst. They are extremely rare in the left upper quadrant, although a few have been reported. What about the area of radiolucency. Is that striking?

Dr. Schatzki: No; not at all. I should not consider it definite.

Dr. Kranes: Other conditions to be mentioned, of course, are retroperitoneal sarcoma and fibroma. It seems to me that any malignant tumor in this area is ruled out by the duration of the disease. The most probable diagnosis, so far as I am concerned, is a large splenic cyst, the result of old trauma.

Dr. Edward B. Benedict: I should think that this might well have been a pancreatic cyst.

Dr. Kranes: That is a perfectly good suggestion. A large cyst in the tail of the pancreas can produce exactly the same picture, and I certainly should have mentioned it; but I see no way of differentiating a splenic and a pancreatic cyst clinically, except that the patient was a woman and had had an injury, two factors more in keeping with splenic cyst than with pancreatic cyst.

Dr. Ellis: This patient came in with a purely mechanical problem. She felt perfectly well and had had no bowel symptoms for many years. At first, of course, we tried to tie this mass in the abdomen with the previous disease, but we could not do it in any way that seemed reasonable. Therefore, it boiled down to the fact that she had a mass in the abdomen. What was it? In addition to the conditions mentioned by Dr. Kranes we thought of amyloid disease. Was this a huge amyloid spleen or liver? There was no positive evidence of amyloid disease in the laboratory tests. We were left with the diagnosis of cyst for the reasons that Dr. Kranes has mentioned. The preoperative diagnosis was cyst of the spleen, pancreas or mesentery, with betting on every one.

Clinical Diagnosis

Cyst of spleen, pancreas or mesentery.

Dr. Kranes's Diagnosis

Cyst of spleen.

Anatomical Diagnosis

Cyst of pancreas.

Pathological Discussion

Dr. Mallory: Dr. Allen, will you discuss the operative findings?

Dr. Arthur W. Allen: Dr. Kranes has discussed the problem presented at the time of this woman's first admission, when she had the short-circuiting procedure, extremely well, and he arrived at as nearly a correct diagnosis as we could obtain from the exploratory operation. We short-circuited the obstructed loop of small intestine, and the pathological diagnosis that was made on the specimen was a nonspecific granulomatous lesion involving the small bowel — Crohn's disease or regional enteritis. She had had a peritonitis preceding or following the first exploration, so at the time of the

short-circuiting procedure it was difficult to re-explore extensively. She was not in good condition, and although we made some effort to discover the mass that had been described in the left upper quadrant, we could not get to it without too much dissection. So we short-circuited the loop, believing that that was all we should do.

She came back the last time with a perfectly huge mass, which could be felt on the left side. It was not hard but felt like a soft cyst. It was an interesting problem, and the various possibilities of cystic mass in this location were, of course, considered. All have been named that we did consider, but in going over the films with Dr. Schatzki I finally decided on the diagnosis of a cyst of the spleen. Cysts of the spleen always occur at a pole, and one had to assume that it was the lower pole of the spleen from which this mass had developed. The reason that it did not extend farther downward was that she had had peritonitis and the adhesions had kept it confined in that direction. It had followed the line of least resistance to fill the whole upper abdomen.

At operation we found that the mass was cystic, as expected, but that it arose from the pancreas. After determining that, we drained the cyst of 5 liters of fluid by suction, incised it and then anastomosed it to a loop of jejunum high up, just beyond the ligament of Treitz, the only piece of normal intestine that we could find nearby.

DR. MALLORY: This operation was essentially an internal marsupialization of the cyst.

DR. ALLEN: We had two choices. The other was to bring the edges of the cyst out through the abdominal wall, hoping that the sinus might eventually close, as they often do; if the sinus did not close, one could then implant the sinus into the intestine. The intestines were so interadherent, with every loop stuck to another, that it was not pleasant to think of having to go back into the abdomen again to implant a sinus tract. Within the last year or two Dr. Ralph Adams,* of the Lahey Clinic, has reported the anastomosis of pancreatic cysts to the small intestine, associated with an enteroenterostomy. We should have liked to do an enteroenterostomy here but could not do it. All we could do was to make an anastomosis to the jejunum. We took out a generous portion of the cyst wall for pathological examination.

DR. MALLORY: A section of the cyst wall showed it to be lined by columnar epithelium, similar in appearance to the lining of the normal pancreatic ducts. This was surrounded by dense fibrous tissue, and in the periphery there were numerous atrophic clusters of pancreatic acini. So we felt quite certain that Dr. Allen was correct in assuming that it had originated in the pancreas.

*Adams, R., and Nishijima, R. A. Surgical treatment of pancreatic cysts. *Surg., Gynec. & Obst.* **83**:181-187, 1946.

CASE 33322

PRESENTATION OF CASE

A forty-year-old housewife entered the hospital because of right chest pain and hemoptyses.

Thirteen years before entry she developed an upper respiratory infection followed by cough, fever and pleuritic pain on the right side. An x-ray film of the chest was said to have shown fluid at the right base. A sputum smear was negative for acid-fast organisms. After several weeks in bed she felt completely well except for a persistent, mild, slightly productive cough, which became accentuated when she had a "cold." Eight years before entry two pregnancies were interrupted on the basis of another chest x-ray film. Four and a half years before entry she began to have hemoptyses. X-ray films at that time revealed no abnormality and sputum examination was negative. Several months later she was admitted to a tuberculosis sanatorium, where x-ray examination revealed a shift of mediastinal contents to the right and considerable soft infiltration in the lower half of the right lung field. One sputum was reported positive, but ten succeeding examinations over the remaining seventeen months' stay at the sanatorium were negative. A right pneumothorax was performed, and this was maintained after discharge for a total of twenty-three months because of continued hemoptyses. Two years before entry she was admitted to another tuberculosis sanatorium, where bronchoscopy revealed that the right main bronchus was practically occluded just below the carina by a whitish tumor, which bled profusely on touching. A biopsy specimen was said to show undifferentiated or small-cell carcinoma. Bronchoscopic electrocoagulation of this tumor was carried out six times, and the patient received several courses of deep x-ray therapy. The hemoptyses, however, still continued. The patient also complained of right anterior chest pain, which was often severe enough to require codein for relief. Exertional dyspnea, easy fatigue, chronic cough and pallor had been present for several years.

On physical examination the patient was pale but appeared to be in no acute distress. The trachea was deviated to the right. The entire right lung field was dull to percussion. Over the upper portion, there was bronchial breathing and tactile fremitus was increased. Over the lower portion, the breath sounds were absent and tactile fremitus was decreased. The heart was shifted to the right. There was a Grade II systolic murmur at the apex. The abdomen and extremities were normal.

The temperature was 98.6°F., the pulse 90, and the respirations 20. The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood showed a red-cell count of 2,500,000 with 6.0 gm. of hemoglobin, and

a white-cell count of 3500, with 75 per cent neutrophils. The urine was normal.

An x-ray film showed the right chest cavity to be smaller than the left. The mediastinum was retracted to the right. The right lung was completely airless except for a small bubble in the right upper chest. The left lung was clear.

Bronchoscopy on the third hospital day was unsuccessful because of profuse hemorrhage. On the sixth hospital day another attempt at bronchoscopy was made. Again there was profuse bronchial hemorrhage, and the patient died suddenly in respiratory failure.

Differential Diagnosis

Dr. Carroll B. Miller: I shall depart from the usual procedure in these case discussions and declare at the start that there can be little doubt that the diagnosis in this case is adenoma of the right main bronchus. I shall then discuss why other diagnoses are unnecessary and unlikely. That there may be other conditions associated with the adenoma warrants mention and deserves consideration, but they would be secondary and probably not necessarily related to the adenoma.

The age of the patient, the sex and the events in the thirteen-year-history of respiratory symptoms indicative of bronchial obstruction and associated collapse, pneumonitis and possibly bronchiectasis all point to an adenoma. Such a tumor has characteristically a long history, and thus, by virtue of its being admittedly a "benign tumor," does not cause progressive systemic decimating effects as are seen in a malignant tumor of the bronchus. Parenthetically, however, if the side effects of retained infection and pulmonary destruction occur in association with an adenoma or if the adenoma undergoes malignant degeneration as it is often claimed, the picture may be indistinguishable from that of a primary bronchiogenic carcinoma.

Three interesting details in the history must be discussed: the suspicion of tuberculosis, the biopsy report after bronchoscopy of carcinoma and the lack of response to x-ray therapy. It is not uncommon for a patient with any lung disease to be suspected of having tuberculous infection, and rightly so. Indeed, this patient's lung may well have shown tuberculosis at post-mortem examination, but that is not an important feature of the case. Hemoptysis, pleural effusion and x-ray signs of a soft infiltration in the right lower lung field are enough to make any diagnostician highly suspicious of tuberculosis, but sputum examinations, with one exception, were repeatedly negative for acid-fast organisms, and when bronchoscopy was finally resorted to, an obstructing tumor was found. The effect of this tumor in the main bronchus was sufficient to account for collapse, pneumonitis, pleural effusion and shift of the mediastinum — in short, the picture that the patient showed on various occasions.

The microscopical diagnosis on biopsy two years previously was "undifferentiated carcinoma," and the tumor failed to respond to x-ray treatment. Without much doubt an undifferentiated carcinoma, thus probably highly malignant, would neither have permitted the patient to live two years nor have failed to show some response to radiation therapy. To quote Boyd's *Surgical Pathology*, "Surface cells [of these adenomas] may undergo squamous metaplasia which may suggest epidermoid carcinoma." Similarly, the nature and arrangement of the cells have sometimes provoked the diagnosis of "alveolar sarcoma, basal cell carcinoma or adenocarcinoma."

Let us consider the physical examination and roentgenologic picture of the patient. She had signs of extensive collapse of the right lung. Laboratory data indicated a probably chronic secondary anemia and tendency toward agranulocytosis, the results of chronic infection.

Taken all together, the history, physical findings, laboratory data, x-ray findings and bronchoscopic reports strongly suggest a benign, massively obstructing tumor of the right main bronchus, and this must have been a bronchial adenoma. Other lesions, such as a nonspecific granuloma, a foreign-body granuloma (the history is negative for aspiration) or a gumma (there is no Hinton report, and I assume that the serologic reaction of the serum was negative), may be dismissed as extremely rare and unlikely. The tumor, unfortunately, was malignant for this patient, since it was responsible for her demise; because of its extreme vascularity, hemorrhages were frequent, as is often the case with adenomas, and the cause of death was undoubtedly an inundation of the left bronchial tree, with consequent suffocation. It is this type of case that makes the surgeon so frequently prefer to proceed with lung resection without the benefit of cytologic examination of the neoplasm, once the gross appearance and site of obstruction have been determined by bronchoscopy.

No discussion of the pathology and surgical treatment of bronchial adenoma is complete without mention of the frequent, almost invariable, dumbbell shape of the tumor, which characteristic justifies the abandonment of treatment by bronchoscopic morcellation and the adoption of resection at the site of that portion of the lung containing and blocked off by the tumor.

Clinical Diagnosis

Bronchial tumor, type undetermined, with recurrent hemorrhages.

Dr. Miller's Diagnoses

Adenoma of right main bronchus, with bronchiectasis.

Hemorrhage into left bronchial system.

Anatomical Diagnosis

Bronchial adenoma of right main bronchus, with hemorrhage into left lung.

Pathological Discussion

Dr. Benjamin Castleman: As Dr. Miller predicted, this patient had a bronchial adenoma. The lumen of the right main bronchus was completely occluded by a pinkish gray tumor (Fig. 1). The tumor was attached to the bronchial wall at a point approximately 1.5 cm. from the bifurcation of the trachea and had grown proximally for a short distance into the trachea and distally into the secondary bronchi to form a large mass 9.5 cm. long and 6.0 cm. in diameter. Nowhere was the bronchial wall destroyed; the tumor merely grew down the lumens in pseudopod formation. Beyond the tumor there was bronchiectasis in the small collapsed lung. The left lung was fluffy, and the bronchi and alveoli were filled with blood — an obvious aspiration of blood from the tumor.

Microscopically the tumor was a typical adenoma, with no evidence of carcinoma. The regional lymph nodes showed chronic inflammation.

Have you any comment, Dr. Benedict?

Dr. Edward B. Benedict: The danger of serious hemorrhage from bronchial adenoma is a real one. If an adenoma completely blocks one main bronchus, it means, of course, that the patient has only one useful lung. If serious hemorrhage occurs, either spontaneously or at the time of a bronchoscopic biopsy, it may mean drowning of the good lung by hemorrhage and a rapidly fatal termination. The experienced bronchoscopist can usually differentiate adenoma from carcinoma by the gross appearance. The former presents a smooth rounded surface,

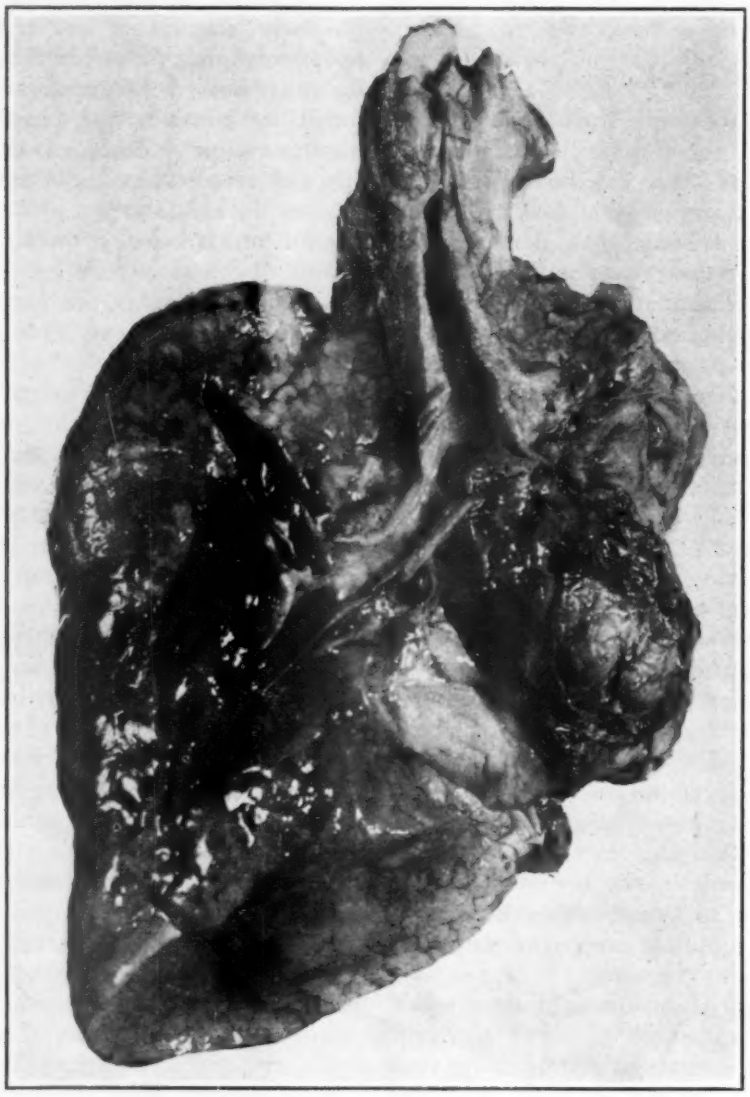

Figure 1.

whereas the latter usually is nodular and irregular. On the other hand, there have been at least two cases of carcinoma in my experience in which a rather smooth polypoid finger-like carcinoma extended upward along the main bronchus, grossly simulating an adenoma. If the bronchoscopist is suspicious of adenoma from a long history of intermittent attacks of bronchial obstruction with repeated hemoptyses and so-called "pneumonia" and if, in addition, he finds a smooth grossly benign-appearing tumor blocking one main bronchus, he might do well to take no biopsy for fear of serious hemorrhage. The surgeon would then probably operate on the basis of the history, the x-ray examination, the gross findings at bronchoscopy and the probability of irreparable lung damage. The bronchoscopist will have done his part by indicating the gross appearance of the tumor and the level at which it appears in the bronchus.

In the case under discussion, although the gross appearance of the tumor was that of a benign adenoma, there had been a previous report of carcinoma. The taking of a biopsy in this particular case, therefore, seemed especially important. Moreover, the tumor's position in this case, lying across the carina, made it somewhat inaccessible to surgical approach. Although many adenomas have been safely biopsied at bronchoscopy and even largely removed bronchoscopically, in retrospect one cannot help wondering what the outcome would have been if a pneumonectomy had been attempted without bronchoscopic biopsy.

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WALTER PRENTICE BOWERS

Walter Prentice Bowers, of whose death on July 22 we are all aware, may well be ranked as the departed dean of the Massachusetts medical profession.

A life-long general practitioner of medicine and honored by Harvard University as such, a former president of the Massachusetts Medical Society and managing editor of the *Journal* for fifteen years, he was a man of stature among us.

To his older colleagues in the Society, he was a thoughtful, kindly friend; to many more, a wise counselor; to the youngest, we trust, an inspiring legend. Like Dr. Samuel Johnson, he kept his friendships in repair, and his benign presence at all except the more recent Council meetings belied his ninety-odd years.

"Know ye not," said David to his servants, "that there is * * * a great man fallen this day * * * ?"

RESEARCH ON THE COMMON COLD

For several years prior to the discovery of the virus of influenza there was considerable interest in the etiology of the common cold. A number of important investigations were reported during that time, particularly by Dochez and his co-workers,[1,2] in New York City and by Long and his collaborators[3] in Baltimore. These studies were necessarily limited in scope and rather laborious, chiefly because of the failure to find a suitable experimental animal that is susceptible to the disease. To be sure, the chimpanzee was found to be susceptible, but that animal is difficult to handle and not readily available in adequate numbers. The use of human volunteers likewise seemed to entail so many difficulties that only a few investigations involving transmission to human subjects were reported. Some success was claimed with cultivation of a virus from the common cold and its propagation in tissue culture,[4] but this was not confirmed by other workers. Meanwhile, the ease with which the viruses of influenza are isolated and manipulated has diverted the attention of many workers to studies with these agents, and a vast amount of information concerning influenzal infections has accumulated.

The recent war stimulated interest in a number of other human diseases that were of major importance and required immediate investigation. Researches on some of these diseases were also hampered by the failure to find suitable experimental animals. Under the impetus of the war, however, it was possible to obtain both funds and human volunteers to carry out fairly elaborate studies on the etiology and transmission of such diseases as infectious hepatitis and primary atypical pneumonia and on the therapeutic efficacy of certain chemical agents in human malaria. In this

country conscientious objectors and inmates of prisons were the main source of such volunteers. The feasibility of using human volunteers rekindled interest in the simple respiratory infections, particularly since the risks involved in acquiring such infections are much less than those that accompany experimental infections with the diseases just mentioned. At least three groups of workers have engaged in such studies on the common cold, and preliminary reports of the results of the work of two of these groups are now available.

Abernethy,[5] of the Commission on Acute Respiratory Diseases, last year reported briefly on the successful transmission of minor respiratory illnesses to a group of human volunteers. He used filtered secretions from two patients who had different types of illness. The first had an incubation period of one or two days and was characterized chiefly by sneezing, nasal obstruction, coryza and cough; in the other, the incubation period was five or six days, sore throat was an outstanding feature, and nasal symptoms were minimal. These infections reproduced the same type of symptoms on transfer of filtered secretions to other volunteers in each instance. There appeared to be no cross immunity, and whereas a partial immunity to the homologous filtrate was demonstrated to the disease having the longer incubation period, no such immunity resulted from the illness with the short incubation period and the predominantly catarrhal symptoms. No illness resulted from inoculation of control filtrates obtained from the subject's own secretions. It was presumed that the agents that produced these two types of illness were filterable viruses.

A brief account of the plan of study and the nature of the work in progress at the Harvard Hospital in England has recently been given.[6] This work was directed chiefly at attempts to cultivate and propagate the virus of the common cold in embryonated hen's eggs. It was calculated that there was about a 75 per cent chance of success with this method, because it had already proved successful in about three fourths of the attempts with sixty other viruses. Human volunteers were used to test the infectivity of the test materials. The source of the infective material was a pool of secretions obtained from twenty boys with colds during an epidemic at Harrow; this had been stored at −76° C. (in carbon dioxide snow).

The first results reported by the British workers indicate that the material retained its infectivity after at least four and a half months' storage at − 76°C., for one month at −10° C. and for three days in an ordinary refrigerator (4° C.). The upper limit of the size of the infective agent was determined by passing it through graded filters, but the lower limit has not yet been defined. The incubation period of the disease produced was found to be two or three days in most subjects, but occasionally it was five or six days.

An interesting feature of the British studies is the source of the volunteers that were obtained. These were recruited at first among students during their holidays, but others readily became available as news of the work spread. The facilities were arranged to care for only twelve pairs of subjects at a time, different groups being started at intervals of two weeks. The success of the recruiting methods and the satisfaction of the volunteers with the way they were treated are attested by the fact that subjects are now booked for many months in advance. Moreover, many of the volunteers have expressed the desire to serve again and have been allowed to do so, but only after a lapse of six months.

Additional researches on the common cold are being carried out in this country by workers of the National Institute of Health under the direction of Dr. Norman Topping.[7] Some of the subjects of these studies are being recruited from inmates of a reformatory. These studies have only recently gotten under way.

All these investigations and others that may be in progress or that are being contemplated hold forth great promise for the solution, in the not too distant future, of many of the problems of the common cold, including its etiology, its epidemiology and perhaps even its treatment and prevention.

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MASSACHUSETTS MEDICAL SOCIETY

BUREAU OF CLINICAL INFORMATION

All secretaries of various medical groups, such as special societies and alumni associations, are requested to notify the Bureau of Clinical Information regarding scheduled meetings, annual dinners and so forth. If such data are on file, it is hoped that duplication of dates can be avoided.

DEATHS

KINLOCH — Raymond A. Kinloch, M.D., of Springfield, died on July 5. He was in his seventy-third year.

Dr. Kinloch received his degree from University of Vermont College of Medicine in 1903. He was a member of the New England Obstetrical and Gynecological Society and a fellow of the American Medical Association.

His widow and a daughter survive.

PREBLE — Wallace Preble, M.D., of Cambridge, died on February 22. He was in his ninetieth year.

Dr. Preble received his degree from Harvard Medical School in 1883.

A daughter survives.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

RELOCATION OF WASSERMANN LABORATORY

The Wassermann Laboratory of the Massachusetts Department of Public Health has been moved to the Bussey Building, 281 South Street, Jamaica Plain, Boston 30. The telephone number of the laboratory is ARNold 1232.

NEW APPOINTMENTS

William D. Wellock, D.M.D., M.P.H., a Navy veteran and a recent graduate of the Harvard School of Public Health, has been appointed director of the Division of Dental Health. His private practice in Boston was interrupted by the outbreak of the war. As a commander in the United States Naval Dental Reserve, Dr. Wellock served in the Alaskan Theater of Operations for more than two years. He received the degree of Master of Public Health from the Harvard School of Public Health following his separation from the Navy. Dr. Wellock succeeds Dr. A. Laurence Corbman, who has heretofore served as acting director of the division.

Grace E. Lutman, M.D., M.P.H., Dr.P.H., a former assistant district state health officer in the New York State Department of Health, has been appointed supervisor of Clinics for Crippled Children. Dr. Lutman will administer the state clinics located in Salem, Brockton, Springfield, Fall River, Pittsfield, Lowell, Haverhill, Hyannis, Worcester, Greenfield and Gardner.

William W. Wood, M.B.A., is serving as survey administrator in the Bureau of Hospital Survey and Construction. A Navy veteran, Mr. Wood saw service in the Atlantic, Pacific, Mediterranean and Caribbean theaters.

Francis W. Hooper, M.D., has been appointed district health officer of the South Metropolitan District, with headquarters located in Quincy. Prior to his appointment, Dr. Hooper saw eighteen months' service in the European Theater of Operations as a captain in the Army Medical Corps. He formerly practiced medicine in Westwood, Massachusetts.

MISCELLANY

NOTES

Dr. Monroe Davis Eaton became associate professor of bacteriology and immunology at Harvard Medical School on July 1. Dr. Eaton was born in Stockton, California, in 1904. He received his collegiate education at Stanford University, where he received an A.B. degree in 1927 and an A.M. degree in 1928. He graduated from Harvard Medical School in 1930, and for three years served as assistant in bacteriology and immunology in that school. Between 1933 and 1936 he was an instructor in bacteriology at Yale University School of Medicine, from 1936 to 1937 he was assistant professor of bacteriology and immunology at Washington University School of Medicine, and in 1937 he became a member of the staff of the International Health Division of the Rockefeller Foundation, as well as director of the Research Laboratory of the California State Department of Public Health.

Dr. Donald G. Anderson, until recently dean of the Boston University School of Medicine, has assumed the post of secretary of the Council on Medical Education and Hospitals of the American Medical Association.

CORRESPONDENCE

DANGERS OF POOLED PLASMA

To the Editor: During the past year, four patients have died at our hospital because of severe liver disease following the infusion of "pooled plasma" at other institutions, and in all cases, the use of plasma had been ill advised. The indications for employing plasma are quite rare. If it must be used, it should be obtained from the blood of an individual donor who can be carefully checked for an antecedent history of jaundice or infectious hepatitis. That plasma is not a substitute for whole blood became obvious in the treatment of war casualties. That "pooled plasma" caused many deaths three to five months after the completion of brilliant surgery during the war years should militate against its use in civilian practice.

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UNAUTHORIZED USE OF CORRESPONDENCE

To the Editor: Recently, physicians in Boston, and possibly elsewhere, were circularized by a pharmaceutical house called the Chal-Yon Corporation. This corporation has launched a campaign advertising a product called Chal-Yon which,

among other things, is said to be effective against fungus infections. Included with a description of the therapeutic accomplishments of their product is a statement bearing my signature and dated August 2, 1946, to the effect that this material is nontoxic. The letter from which this statement was taken was addressed to an individual in response to his inquiries whether, in my opinion, the material was nontoxic.

In the statement that appears with the advertisement, my letterhead and signature are carefully reproduced but other parts are conveniently deleted. This abbreviated letter was distributed by the Chal-Yon Corporation, the existence of which I was entirely unaware (if, in fact, it did exist at all at the time) until the letter made its appearance in the mails. The effect of the letter is such that it appears to be a signed statement of indorsement, not only by me but also by my associates, whose names appear on the letterhead.

I wish to inform those physicians who have received the circular that the use of this statement was entirely unauthorized; it was written to an individual and was in no way intended as an indorsement of the product recently advertised.

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BOOK REVIEWS

Acetanilid: A critical bibliographic review. By Martin Gross, M.D. With an introduction by Howard W. Haggard, M.D. 8°, cloth, 155 pp., with 8 illustrations. New Haven, Connecticut: Hillhouse Press, 1946. $3.00.

The appearance of many sensational articles in the press regarding certain generally used drugs — acetanilid, for example — has led to considerable discussion, some of it unscientific, and to controversial utterances by authorities concerning the difficulties and dangers in the use of this drug.

This book takes a step toward fact finding in the field of the intoxications, in which emotional attitudes and neglect of human factors have held sway in the past. Dr. Gross reviews the literature and includes a full-length view of what acetanilid is and incidentally what it is not, described in terms of what acetanilid does and does not do. He does not minimize the difficulties in — and the necessity of — determining exactly how toxic acetanilid is — a matter that has been grossly obscured by uncritical alarmists in the past, who have attributed to that drug alone the complicated end-results of deficiency disease, chronic alcoholic addiction and various psychologic disorders that long antedated the ingestion of acetanilid. He points out its place in medicine, and outlines broadly its effectiveness as an analgesic.

This book does not contain a host of fresh facts. Rather, it reinterprets many of the older and basic articles on acetanilid in the more recent light of psychologic and psychosomatic medicine. The best chapter deals with the question of addiction to acetanilid, a minor problem according to this author's figures. This chapter summarizes the whole problem of addiction and habituation in general, as well as the particular aspects that apply to acetanilid.

Medical Education and the Changing Order. By Raymond B. Allen, M.D., Ph.D. Studies of the New York Academy of Medicine, Committee on Medicine and the Changing Order. 8°, cloth, 142 pp. New York: The Commonwealth Fund, 1946. $1.50.

Dr. Allen is executive dean of the College of Dentistry, Medicine and Pharmacy of the University of Illinois. His monograph was prepared under the auspices of the Committee on Medicine and the Changing Order established by the New York Academy of Medicine and is one of a series, each one of which is interesting.

The author presents a readable account of medical education, describing first its historical background and later following the trends that have appeared to modify its course. His comments are shrewd and searching; he agrees with most medical educators that it appears difficult to attract to the study of medicine as high a type of student as is desirable because, in part, of the high cost in time and money. He gives many hints about medical education and how to make it more useful. He suggests, for example, that the curriculum is not entirely perfect, that pedagogic methods employed are not wholly adequate and that many internships — admittedly a vital part of a doctor's education — are not all they might be.

Dr. Allen concludes with a forecast: the cost of medical education will not diminish; there is no more crucial problem facing medical care than the distribution of doctors; and that, although in the past the services of medicine, like those of religion, have been largely personal and although there will always be a need for personal services, medicine of the future, if it is to progress as a social as well as a biologic science, must broaden its outlook and adjust its educational program accordingly.

The Centennial of Surgical Anesthesia: An annotated catalogue of books and pamphlets bearing on the early history of surgical anesthesia. Compiled by John F. Fulton, M.D., and Madeline E. Stanton, A.B. 8°, paper, 102 pp., with 8 facsimiles and one portrait. New York: Henry Schuman, 1946. $4.00.

The compilers of this catalogue have assembled an excellent collection of literary material on the subject of surgical anesthesia. The period covered is from the time of Pliny and Dioscorides (A.D. 50 to 100) to the discovery of the use of ether in the United States in 1842–1846 and of chloroform in England in 1847 and to the rediscovery of nitrous oxide in 1863. The catalogue is divided into eight major divisions, with a short historical introduction to each division, and the major items are annotated. The catalogue is limited to items exhibited at the Yale Medical Library in October, 1946, either in the original or in facsimile. Naturally, emphasis is placed on experimental work in the United States.

The first section concerns the forerunners of surgical anesthesia and includes the Greek and Roman authors and their references to mandragora and the soporific sponge, the use of physical agents, such as the snow and ice-cold water of Avicenna and Severinus, and the method of nerve compression of James Moore (1784), nitrous oxide, carbon dioxide and the anesthetic agents, mesmerism and hypnotism and the early writings of Cordus (1561) and Turner (1743) on sulfuric ether. Subsequent sections are devoted to the American claimants of the discovery of surgical anesthesia: Crawford W. Long, Horace Wells, William T. G. Morton and Charles T. Jackson. Each lists in detail the original papers of the author, and title pages are reproduced in facsimile. The story of the controversy is presented in a factual manner without an endeavor to pass judgment on the merits of the matter. To each of these divisions is appended a list of references on biography and commentaries.

A large section, which is concerned with the writings of and about Morton, includes a census of the known copies of the Morton publications. (Since the publication of this catalogue, the Boston Medical Library has acquired a copy of the rare third edition of Morton's fourteen-page *Letheon*, the earliest of this series to be located in any collection, public or private.)

Another section describes the discovery of chloroform and its use by Sir James Y. Simpson. During 1847 and 1848 the medical literature of the world became flooded with articles about ether anesthesia, and in 1848 about chloroform. The seventh section comprises a list of references to publications of this period on ether, chloroform and other agents, including opiates and nitrous oxide, and mesmerism, followed by a short list of early general monographs on surgical anesthesia and a note on anesthesia and psychiatry in which is described *The Anesthetic Revelation and the Gist of Philosophy* (1847) by Benjamin P. Blood. The concluding section comprises a long list of journal articles, monographs and addresses on the history of the subject.

The catalogue is printed and published in a de luxe manner and should be in all medical-history collections.

The Diagnosis and Treatment of Bronchial Asthma. By Leslie W. Gay, Ph.D., M.D. With a foreword by Warfield R. Longcope, M.D. 8°, cloth, 334 pp., with 80 illustrations, 5 plates and 39 tables. Baltimore: Williams and Wilkins Company, 1946. $5.00.

In recent years a number of encyclopedic books have been published on allergic diseases. Brief summaries are contained in systems of medicine. Dr. Gay has written a book

on bronchial asthma that fits between these extremes. The author, with a quarter century of experience in allergy, has compiled a text useful for the medical student and the internist. The approach to the problem of the study of the asthmatic patient is adequately presented. The author stresses the value of an adequate history; the listing of case types aids in the classification of the new patient. Skin tests are placed on a par with other laboratory procedures in allergic investigation. They supplement, but in no way replace, a detailed history.

Psychosomatic influences on the asthmatic state command an entire chapter. These influences are usually considered in the everyday treatment of the disease but are rarely mentioned in the literature. The author devotes sufficient space for a review of the literature and presentation of his opinion and experience.

The remaining chapters outline the author's plan of treatment for the asthmatic state. This section suffers somewhat from the detail of certain procedures now infrequently used. Nevertheless, the various types of therapy are discussed clearly and authoritatively. Case studies in the text are judiciously placed and amply illustrate and emphasize the author's text.

Scientists against Time. By James Phinney Baxter, 3rd. 8°, cloth, 473 pp., with 74 illustrations. Boston: Little, Brown and Company, 1946. $5.00.

In this book Mr. Baxter tells the inside story of the Office of Scientific Research and Development (O.S.R.D.) of World War II. He presents an account of all the marvelous inventions employed in combat and defense — radar and loran, rockets, fire control, proximity fuzes, the Dukw and Weasel and the atomic bomb. The modern aspects of submarine, amphibious, naval and air warfare and the new chemical achievements in explosives and propellants, smoke, incendiaries and flame throwers are discussed at length. A chapter entitled "Military Medicine" considers antimalarial drugs, blood and blood substitutes, penicillin, insecticides and rodenticides and aviation medicine. The use of quinine, plasmochin, quinacrine and chloroquine in the treatment and prevention of malaria, as well as the experimental research on other antimalarials, are described in detail. In the chapter on insecticides is told the story of DDT and its successful use in the camp and field. A chapter is devoted to a summary of the operations research of O.S.R.D. to May 1, 1943.

The text is well written in an easy, interesting style, the material is well organized, and the book is well published in every way. The contract with the publishers is for ten years, after which the book becomes the property of the public domain. It is recommended for all medical, scientific and public libraries and should prove of universal interest.

Conduction Anesthesia: Clinical studies of George P. Pitkin, M.D. Edited by James L. Southworth, M.D., and Robert A. Hingson, M.D. 4°, cloth, 981 pp., with 606 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $18.00.

This volume, edited by Southworth and Hingson with the help of eight collaborators, represents a real contribution to the field of modern anesthesiology and is a fitting tribute to the late Dr. George P. Pitkin. The general arrangement of the book, its wealth of excellent illustrations and its numerous references make it desirable for both the student and the specialist. Chapters on the cranial and spinal nerves and the autonomic nervous system, exceedingly well done, provide a real understanding of the subject, which is so necessary for the successful clinical application of conduction anesthesia. The descriptive material found in these chapters, in addition to the beautiful and carefully labeled anatomic drawings, leaves little to be desired.

The inclusion of chapters on therapeutic nerve block, refrigeration anesthesia and continuous spinal and caudal anesthesia places the necessary emphasis on modern developments in this branch of anesthesiology. The chapter on pharmacology and toxicology of cocaine and the synthetic local anesthetics comprises an excellent review of this basic material. A special section devoted to shock will be welcomed by the anesthesiologist who must either plan to prevent or occasionally to treat this condition in his daily practice.

The largest single part of the book deals with the principles of conduction anesthesia and their application in the various regions of the body. This section is most complete with scores of fine illustrations, and woven through it are the ideas and technics of Dr. Pitkin, who, during his life, did so much to popularize on a sound basis spinal and other forms of regional anesthesia.

White Caps: The story of nursing. By Victor Robinson, M.D. 8°, cloth, 425 pp., with 24 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $3.75.

Dr. Robinson has written a comprehensive history of nursing in all its aspects from the earliest times to World War II.

The early chapters, which have to do with the period of antiquity and the Middle Ages, relate the part that the Jews, Buddhists, Greeks, Romans and French, including the Augustinian nuns of the Hôtel-Dieu, played in the care of the sick in those times. The Ladies of Charity of the order of St. Vincent de Paul of the seventeenth century and nursing in the eighteenth century follow, with a special chapter on Florence Nightingale. Special emphasis is placed on American nursing from the time of the Puritans through World War II. Bridget Fuller, wife of Deacon Samuel Fuller, was the first midwife in Plymouth Colony, the deacon having been the first physician. Nursing in the Revolution, the War of 1812 and the Civil War are then depicted, the highlights in the careers of such pioneers as Elizabeth Blackwell, Dorothea Lynde Dix and Mary Ann Bell Bickerdyke being presented. The American story is completed with chapters on Clara Barton, on the training of the American nurse in the period 1863–1943 and on nursing in World War II. Special chapters are devoted to Edith Cavell, of World War I, and to the nursing sisters of the Soviet Union. The history concludes with a chapter on statistics and a valuable chronology of nursing events.

The material is well organized and the text written in an interesting narrative style. The type is good, and the paper soft and pleasing to the eye. A good index is appended to the text. This book is recommended for all libraries, medical and public, and all historical collections.

Medical Research: A symposium. Edited by Austin Smith, M.D. 8°, cloth, 169 pp., with 17 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $5.00.

This book contains eight essays that deal with the importance of medical research. The contributors comprise a distinguished group including, among others, such well known writers as Walter C. Alvarez, Morris Fishbein and Torald Sollmann. Each essay tells an interesting story, emphasizing the need for research, its fertility and why its futherance is required. On the whole, the book is the kind of textbook that hospital or medical-school trustees should study and is likely to be fully as interesting to them as to physicians. Anyone will find the last essay good reading: it describes medical photography and is illustrated with convincing and graphic reproductions.

NOTICES

COLLEGE OF PHYSICIANS FELLOWSHIPS

The American College of Physicians has announced that a limited number of fellowships in medicine will be available from July 1, 1948, to June 30, 1949. These fellowships are designed to provide an opportunity for research training either in the basic medical sciences or in the application of these sciences to clinical investigation. They are for the benefit of physicians who are in the early stages of their preparation for a teaching and investigative career in internal medicine. Assurance must be provided that the applicant will be acceptable in the laboratory or clinic of his choice and that he will be provided with the facilities necessary for the proper pursuit of his work. The stipend will be from $2,200 to $3,000. Application forms will be supplied on request to the American College of Physicians, 4200 Pine Street, Philadelphia 4. Applications must be submitted in duplicate not later than November 1, 1947.

(*Notices continued on page xv*)